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MEDICINE IN THE TEACHING HOSPITAL OF TODAY AND TOMORROW

Walter Bauer, M.D., Boston

Good medical care must still depend on the dedicated and well-trained physician. The integration of medicine depends on the integration of medical teachers. The educational experiment here described involved the creation of integrated units within a teaching hospital, each unit being a miniature department of medicine made up of full-time and part-time physicians, clinical investigators, and, in some instances, basic scientists. The units are devoted to such fields as hematology, gastroenterology, and cardiology, and the arrangement is not to be confused with the division of a hospital into arthritis wards, gastroenterology wards, pulmonary disease wards, and so on. The unit team plan provides superb opportunities for broadening the viewpoints of medical students and house staff alike. Teaching is improved, research is stimulated, and the purpose of the whole enterprise, to give the individual patient the best possible care, is constantly kept in view.

TO SERVE as president of the Association of American Physicians is both an honor and a privilege. My most awesome duty has been this presidential address. I found it an even more lonely task than had been expected. Not until my thoughts and ideals were shared with some of my colleagues did the experience become rewarding. On reviewing the pace of human progress and the many resulting problems, one becomes increasingly aware that the potentiality for future progress has never been so great. There is, however, a wide disparity between achievement and potential. It is this theme that I wish to develop.

We are living in an exciting period of great change and transition. Contemporary political, cultural, economic, and scientific upheaval is affecting every facet of human existence—and in no sphere, I submit, are these forces more complexly interwoven than in the science, or art, or profession of medicine in the world of today. Yes, the circumstances of daily life are changing more rapidly than they have ever changed before in man's experience. We must reckon with these many forces if we are to supply stability of purpose to our teaching hospitals. We must also be promptly and delicately responsive to changes in our environment as well as to changes in objectives.

I should like to discuss certain aspects of this problem as they concern medicine, for I feel deeply that some of our difficulties may be unique to our times and that the moment is at hand for forthright consideration of how best to meet them now and in the future. I will address myself to some of the problems now facing the university teaching hospital and its department of medicine.

Jackson Professor of Clinical Medicine, Harvard Medical School, and Chief of the Medical Services, Massachusetts General Hospital.
Presidential address, read before the Association of American Physicians, Atlantic City, May 5, 1959.

We must keep in mind the special role of the teaching hospital in contemporary medicine. Its function is a creative one. Here, new physicians are trained and graduated. Here, the character and content of medical practice are continuously reshaped as new researches are conducted and new ideas are conceived and tested. And here, last but not least, the patient is cared for in a manner that not only gives him the best that medicine has to offer but also displays a standard and style of care that students and house staff may strive to emulate in the years beyond their training. This should be patient care in medicine's grand tradition, embodying humanity, wisdom, dignity, and compassion. But it is something more; it is razor-edged scientific analysis, probing, observing, recording, doubting, alert to every aberration—from the patient's demeanor to the enzymes in his serum. The teaching hospital does indeed have a special creative role, placing on it responsibilities, both grave and inescapable. What we do and think in our teaching hospitals will influence the thought and practice of our colleagues everywhere and, in turn, the health and happiness of our generation.

Current Problems

The great problem we now face is: How can we provide and maintain a properly balanced program of patient care, teaching, and research in the face of the torrential outpouring of new knowledge? Much of this knowledge has clear relevance for medicine, and more could have relevance if the right person were on hand to perceive and exploit its latent importance. Problems never come earmarked as problems. How, then, can we investigate an unknown in medicine if it has to be approached in biochemical terms by men who must both recognize a clinical problem and conceive a biochemical solution? If we are to promote meaningful and competent research at the more fundamental levels of biological organization, how can we simultaneously imbue our students with the chief humanistic aim of medicine—which is, that the patient's interest comes first and the investigator's second? How can we best integrate the new movement in scientific medicine with the work and thought of our experienced clinicians, who may be alienated by its esoteric techniques and minute concern with the capers of carbon atoms?

These are the questions to be answered and the problems to be faced. Few would deny the major premise that a new scientific revolution is upon us. Starting soon after World War II, there has occurred an incredible output of basic biological research in fields adjacent to or potentially adjacent to medicine. The factors inciting this revolution—the advent of radioactive isotopes, perfection of chromatographic procedures and methods of protein purification, increased financial support of research, etc.—are beyond the scope of this discussion. Suffice it to say that many of our young physicians have participated in this development. Some of them have had a period of formal scientific training at our universities or similar institutions. Others have somehow managed to train themselves in scientific disciplines even while working in clinical areas. This is mirrored in our medical journals and the content of our research meetings—fully illustrated by yesterday's program, where we noted that "the syndrome" is giving way to what might be called "the gospel according to Saint Geiger."

We are standing in the middle of what might reasonably be called a blizzard of scientific progress. The rate at which progress is being made has led to increasing difficulty in keeping abreast of the published reports of that progress. The inevitable consequences have been an increase in specialization, a tendency toward separation of practice from research, and, as some would say, the invasion of one field by persons whose backgrounds and training have been in other areas. In addition to this increase in specialization, there has arisen an increasing difficulty of communication not only between persons in different scientific disciplines but also between persons within a given field. How, in the face of these difficulties, can we achieve and maintain a high standard of patient care, teaching, and research—a *modus operandi* which will enable us to preserve the unity of the whole of internal medicine? How can we mount this whirlwind and make it take us where we want to go? I am sure there are no right answers to these questions—that is, no answers that are right for each department of medicine or for each member of such a department.

An Experiment in Medicine

The major purpose of our annual meeting is to consider together the results and implications of experimental medicine. Because of this, I am encouraged to outline for you, in the form of a progress report, the results of an experiment in progress at the Massachusetts General Hospital—an experiment in how to accommodate ourselves most effectively to meet the challenges and opportunities of present-day academic medicine. The approach which I shall outline is neither new nor unique, and the validity of its results can never be unassailably fortified with the armor of standard deviations and chi squares. Nevertheless, I am convinced that this experiment or some parallel approach must be vigorously pursued in every teaching hospital.

This program has been based on two general premises. The first is that specialization is necessary and that it is here to stay. Himsworth has phrased this point aptly:

> The present situation has arisen because medical knowledge has grown to such an extent that it is no longer, and never again will be, within the capacity of any individual man to master more than a small fraction of it. Specialization has become a necessity. To decry this not only ignores fact; it is to deny the very means that have made our recent progress possible. Specialization is a natural phenomenon. It is comparable in human affairs to differentiation of function in biology. . . . It is the same with human organizations.

Specialization holds out to them—be they intellectual or social—the promise of vast extensions in power; but it does so only on condition that integration keeps pace with specialization.

According to Himsworth, then, the difficulties arise not from specialization but from failure of integration. This leads to our second general premise—that integration must exist both among and within individual persons, particularly those key men who lead team efforts. Unless it does, the results may be disappointing.

Units in Medical Service.—Our medical service is composed of autonomous units, each covering one of the specialties of internal medicine. We have a hematology unit, a gastroenterology unit, a cardiology unit, and various others—12 in all—covering most of the categories into which internal medicine has been divided.

In medicine, as in all of biology, we are primarily concerned with the details of structure and its relationship to function. Therefore, one may well ask: "What is the composition of these specialty units, what responsibilities do they assume within the department of medicine, and how do their structures help them to attain their avowed goals?"

Each unit is a group, of variable but workable size, made up of full-time and part-time physicians, clinical investigators, and, in some instances, basic scientists. Dr. Dana M. Atchley, in a personal communication, has written as follows: "I think we should speak of the 'clinical scientist' and the 'basic scientist' because no clinician these days can be a good clinician if he is not a scientist in his attitudes and training."

Each unit must serve as a miniature department of medicine, dedicated to total competence within its designated area of interest. The sweep of its activities must carry from basic laboratory research to the imaginative application of its discipline to the cure of the ill. This is no less than an injunction to these units to maintain a high standard of excellence in mastering the skills of their specialty areas, in applying these skills effectively, in the acquisition of new facts, and in the teaching of its discipline to other students of medicine.

Functions of the Units.—Where can the harassed chief of a medical service find a physician to carry out all of these activities effectively within a specialty area? In American medicine—the answer comes back clearly—it is "nowhere." A specialty unit can no longer be the lengthening shadow of one gifted person, miraculously adapted to the laboratory, the lecture hall, and the clinic. Basic laboratory research in all medical specialties obsessively demands the devoted attention of first-rate minds for maximal returns. Alternatively, seasoned clinical wisdom based on critical evaluation of experience, which is the hallmark of the excellent physician, cannot be acquired as a gratuitous by-product of laboratory research. Proficiency in clinical medicine is painfully acquired and must be constantly cultivated or else it degenerates into the marketing of shopworn sophistries. Faced with this dilemma, we have accepted the fact that it is the unit, not the person, which must responsibly insure the pursuit of medicine in its broadest sense as an area of both theoretical and applied biology.

How is this carried out in practice? One of our smallest units, for example, is composed of physicians who have had extensive training in organic or biological chemistry, physicians who have had experience in the physiological and metabolic techniques of classic clinical research, and clinicians in private practice who maintain an interest in this medical specialty. The weekly activities of this unit attempt to correlate these various approaches. There is a seminar at which the basic scientific foundations of the discipline are explored, led by either a member of the unit or a guest speaker. The unit holds its own weekly "grand rounds" at which the clinical problems of one or two patients are explored in detail, attempting the most precise scientific analysis of the illness, its pathogenesis, and treatment. Finally, there is a specialty clinic and a consultation round at which a large number of specific clinical problems are met in the daily evaluation and care of patients. All of these functions are attended by students and all members of the unit, irrespective of their primary interests. Each makes his major contribution within the area of his greatest competency but serves further to challenge the accuracy and significance of observations and traditional teaching of the other areas of the discipline.

One of the larger groups, the connective tissue unit, is comprised of persons representing a wide variety of backgrounds and disciplines, who share a common interest in the connective tissue, its components, and its diseases. Senior members include practicing physicians, four clinical investigators, a biologist, a protein chemist, and an organic chemist interested primarily in the carbohydrates. Together with a number of clinical and research fellows and students, these persons share the responsibilities previously mentioned and, of course, conduct their own research.

The physician members of each unit also visit on the general medical wards and participate in the teaching of general internal medicine to second-year, third-year, and fourth-year students. Each of the senior investigators is responsible for determining the direction of, and conduct of, his own research work. Collaborative research problems are undertaken when they spring from common interest.

To present one's work and ideas, either formally in a conference or informally over a cup of coffee, before this group of persons whose interest is keen and whose backgrounds are so varied, has proved to be a privilege which each member values above all others.

Value of Unit System.—Is such a unit just another malignant example of the "togetherness" so increasingly evident on the contemporary American scene? Does any interreaction occur when the

scientist and the clinician are brought together? Here lies the crux of the problem. For the successful functioning of this system, we have attempted to appoint a particular type of man to head each unit —a man who by some means has managed to plant a solid foot in a scientific discipline beyond the scope of clinical medicine, generally in biochemistry, biophysics, or physiology. I have the strong conviction that in the careful selection of unit heads lies the key to the success of this plan. By combining clinical medicine and basic science in their training, and by displaying superior competence in both fields, they represent a new breed of physician. Just as the biochemist once was a strange breed, trained in both chemistry and biology, he managed, nevertheless, to survive and flourish. Likewise, this new breed of physician, born of necessity, the product of modern medicine's complexity, will also survive and flourish. They will flourish along with their conventionally trained colleagues—in teaching hospitals where, we hope, their unique viewpoint will promote strong leadership and progress. They will respect the achievements of the clinicians and talk their language. Their scientific background and training should enable them to produce research of competence, comparable to that of the nonclinically trained scientist.

It is true that such men are hard to find, and a chief of medicine who wishes to develop a unit system of this sort must take the time and make the effort to find, to nurture, and to encourage this small but important group of young physicians who show promise of development in this direction. This may be one of his most important responsibilities. Equally important, he must also recruit the much-needed quota of able part-time physicians—clinicians who, because of previous training, wish to maintain an interest in a given medical specialty, as well as to participate in the teaching of students and house staff. He must also do everything in his power to attract top-flight scientists.

Through the efforts of such people, it should be possible to mount a team effort that will develop cohesion and direction. We, at the hospital, like to think of each unit as a balanced one, with due attention paid to all levels of work. Each member should select and occupy his own position in the spectrum, from pure science to clinical medicine, and should command respect for his abilities and accomplishments. We would like to believe that in such units the whole may be greater than the sum of its parts. There should be little room in such units for suspicions and condescending attitudes so often marring the relationships between scientists and clinicians.

In this way, viewpoints can be shared, horizons broadened, and opportunities increased for individuality and self-development. By cooperative effort, members of a unit may take time off in sabbatical leaves or other changes of pace, so necessary for the maintenance of a fresh point of view. In this way, a better appreciation of the many roads that lead to medical knowledge may be achieved. It is already becoming clear from our experience with this plan how exciting and fruitful the results of such team efforts can be when guided by the sort of men about whom I have been talking.

Relationship of Units.—You may well ask how these units relate to one another and function as an integrated department of medicine. The head of the department meets with the chiefs of units at stated intervals. Here, problems are aired with candor and sometimes heat. This not only helps us in effecting unity of purpose in the care of patients and teaching but also familiarizes each unit with the research interests and aims of the others. These and other regularly held exercises help to further our common objectives without encroaching on individuality of expression or action.

Such a department of medicine has all the specialty subdivisions in medicine for purposes of investigation and teaching, yet the foundation of internal medicine is the general medical ward in which all of the various specialty members participate in the care of the sick, no matter whether the patients have the diseases in which they are well versed. It is the general medical ward that is the basic area of integration, both of the person and of the discipline itself. I, personally, deplore the departments of medicine that have arthritis wards, gastroenterology wards, pulmonary disease wards, and others, and distribute their patients on admission to these specialized services. In my opinion, medicine cannot be done that way in the last analysis. It can be and must be studied in the specialty areas, but the care of the patient in the final integration has to be done by an internist working in a general medical service. I emphasize this point because there is a trend in the other direction in the United States and abroad.

Effective Hospital Program

We return, then, to our original question: How can a teaching hospital effectively carry out a program of medical care, teaching, and research? How does the integration achieved in the units help in the pursuit of these three goals? Let us consider them one by one.

Teaching.—As for teaching, the exposure to the unit teams provides superb opportunities for building into medical students and house staff a broad point of view. We have long since conceded that the undergraduate phase of medical education can no longer turn out physicians ready for the practice of medicine. It has to be satisfied with the building of general competence, leaving the acquisition of special knowledge and skills to the graduate training program—especially residency training. Much has been written in recent years about integrating the medical curriculum. Is it not reasonable to

expect that this goal will be more closely approached if our teachers are better integrated? This must surely be a prerequisite for the success of an integrated curriculum, no matter how carefully it is planned.

Education is a simple process. It begins when two people of different life experiences meet and talk. It is this communication between those who are willing to learn from one another which is the essence of the educational experience. Obviously, we cannot teach our patients all of medicine. What we can teach them, however, is the habit of being self-taught. As has recently been said, "It is our job as educators to see to it that our students, on graduation, be not rifle bullets, constantly decelerating, but self-propelled missiles."

Research.—What about research—such an essential component of the modern university medical center? As physicians dedicated to the prevention and treatment of disease, we are vitally interested in furthering this goal. This we can attain by a better understanding of our patients, their diseases, their disturbed physiology, the biology of the involved tissue, and the chemistry and/or biology of potential etiological agents. Having assumed responsibility for teaching, we must imbue our students with an intellectual curiosity at all these levels. Finally, what better antidote for the dangers of cant and dogmatism than research? The unfounded statement, the unsupported conviction, or the traditional belief are not likely to survive long in the questioning attitude engendered by research. To paraphrase an Elizabethan dramatist—research does make better doctors of us all.

Most medical research can be carried out more effectively within a teaching hospital than in a research institute devoid of an association with medical care and teaching. This is obviously true for traditional clinical research, of whatever variety. It is becoming increasingly evident that this is also true for the more basic scientific disciplines. In recognition of this fact, research institutes such as the Rockefeller Institute and the National Institutes of Health have seen fit to provide themselves with hospital facilities to further their research programs. Within the hospital setting the scientist is made constantly aware of the problems involved in medical care while being stimulated by association with students and physicians concerned with the validity and application of medical knowledge. It is our hope that more scientists will do their research in hospitals. If they do, the unit system may be the means by which they will become aware of the unsolved problems of clinical medicine. We also hope that our units will attract scientists to their units, for this would add as much to medicine as it would to science.

Fundamental research should be an integral part of the modern teaching hospital and can no longer be considered a luxury. The full-time scientist in the hospital must be regarded as the professional equal of the clinician and not his handmaiden. We trust that some of these important men will wish to remain permanently in the hospital research setting. Undoubtedly, some will return to other academic departments in medical schools and universities, carrying with them a new awareness of the applicability disciplines to medicine.

Medical Care.—Finally, last to be mentioned but surely not least, we come to patient care—the goal and purpose of the whole complicated enterprise. This remains our primary concern. There are many opportunities in this area for self-delusion and cant. We must impress on our students and house staff the importance of thinking of each patient as a whole human being, a man or a woman of certain social and economic background, with hopes and fears and feelings of guilt and pride. Students so indoctrinated will be mindful of the fact that all the symptoms of a given patient are not necessarily due to a genetically determined enzyme deficiency, however crisply revealed before our eyes by the incontestable techniques of biochemistry. Unless our students are so trained, they will not bring to bear in future years the wisdom and vision needed in helping patients attain better health and more happiness.

We must face this problem honestly. We must avoid the pitfalls of lip service and inconsistency. Here again the unit system can be of help. Beyond the scope of any single person, it has the potential for demonstrating that no sharp boundaries can be drawn between the scientific analysis of disease and the compassionate care of the sick. We trust that unit chiefs will always keep clearly in mind that the primary concern of a teaching hospital is the care of the sick and that it is within this framework that the activities of the unit must be carried out. For the same reasons they should be aware that the definition of good medical care is as elusive as good medical care itself. Whatever criteria we use must constantly be reviewed and rigorously judged from the standpoint of their effects on the patient rather than on the education or convenience of the physician.

Good medical care, even in a scientific age, must still depend on the dedicated and well-trained physician. If we cultivate this attitude and create an environment in which it is commonplace, our medical students should learn that a good medical history is characterized as much by detailed knowledge of the personality of the patient as by an accurate analysis of the physical manifestations of his disease. With interest focused on the individual person, our goals must still be health and happiness. Each member of our house staff must still keep one thought uppermost as he approaches each new patient: How can I help this patient, and as I do so, what can I learn?

32 Fruit St. (14).

DIAGNOSIS OF LEFT-SIDED SUBPHRENIC ABSCESS

Capt. Martin C. Rosner
and
Capt. Morton A. Bosniak, (MC), U. S. A. F.

A patient who had undergone two laparotomies progressed well until the 11th day after the second operation; removal of a drain on that day was followed by fever, pain, and other symptoms suggesting the presence of an abscess. The location of the abscess under the left hemidiaphragm was revealed by roentgenography after the stomach had been moderately distended by having the patient drink a carbonated beverage. The abscess was then drained at a third laparotomy. All infection was cleared by therapy with chloramphenicol, and the patient recovered. Filling the stomach with air and carbon dioxide has certain advantages over filling with barium sulfate. In this case the altered contour of the stomach settled the diagnosis, and the same technique made it possible to follow the recovery process.

Prior to the advent of chemotherapy and antibiotics the diagnosis of subphrenic abscess was indeed a grim one, and all too often made only at autopsy. Ochsner and De Bakey [1] reported 985 deaths in 1,096 patients (89.8%) not subjected to operation, whereas there were 637 deaths among 1,492 patients (32.8%) in whom operation was performed. Numerous authors have emphasized the even graver difficulties associated with left-sided subphrenic abscess. Although roughly 25% of subphrenic abscesses are on the left side, clinicians have been inclined to disregard this variety and discard the diagnosis of subdiaphragmatic suppuration when a right-sided subphrenic abscess has been excluded. Because of the mobility of the structures situated beneath the left side of the diaphragm the characteristic clinical signs may be difficult to elucidate. Yet this very feature promotes a burrowing, multiloculated kind of abscess, with a tendency to rupture into the thorax or abdominal viscera, accounting for the higher over-all mortality in the left-sided as opposed to the right-sided lesions; thus Neuhof and Schlossmann [2] cited a 75% mortality in the former contrasted with 35% in the latter.

Since the inception of antibiotic therapy survey of the literature reveals a striking paucity of commentary on subphrenic abscess; but Rabin,[3] writing in 1951, stated, "The use of chemotherapy and antibiotics in recent years has diminished the number of cases of subphrenic abscess, but the mortality generally still remains high and the course after drainage, prolonged. . . . Although these drugs have diminished the number of cases of subphrenic abscess, they have also increased the number in which the onset is insidious."

The purpose of this paper is to present a typical case of left-sided subphrenic abscess, with a brief review of the diagnostic criteria, clinical and roentgenographic, and a suggested modification in roentgenologic technique which may aid in the diagnosis; it is hoped thereby to call fresh attention to a serious condition, which, although less frequently encountered than in the past, may be all the more difficult to diagnose.

Report of a Case

A 37-year-old staff sergeant was admitted for the second time to the 7510th U. S. A. F. Hospital on Sept. 2, 1958, with epigastric pain and tenderness relieved by alkali or food. A duodenal ulcer had been demonstrated roentgenographically in 1954 and again in December, 1957. The patient had undergone periods of intensive therapy with proper diet and antacid and antispasmodic medication, but his symptoms recurred, persisted, and increased up to the time of the present admission. There was no history of significant disease, and admission physical examination of this tall, asthenic man was unrevealing except for mild epigastric tenderness; results of blood cell count, fasting blood sugar and blood urea nitrogen level determinations, urinalysis, chest x-ray, and electrocardiogram were within normal limits. A final trial of medical therapy was unsuccessful in completely relieving his pain, and a gastrointestinal series revealed the suspected posterior penetrating duodenal ulcer. He was transferred to the surgical service and subjected to a 70% gastric resection on Sept. 25. On Oct. 4 the patient developed cramping epigastric pain and vomiting with the roentgenographic picture of mechanical obstruction of the small intestine; after intubation failed to relieve the obstruction, laparotomy was performed with lysis of adhesions. Postoperatively the patient was placed on therapy with 600,000 units of procaine penicillin and 0.5

Assistant Chief, Medical Service (Captain Rosner), and Chief, Radiology Service (Captain Bosniak), 7510th U. S. A. F. Hospital. Captain Bosniak is now at the Department of Radiology, New York Hospital–Cornell Medical Center, New York.

Gm. of streptomycin twice a day, and he remained afebrile and progressed satisfactorily. The antibiotic therapy was discontinued after four days.

On Oct. 15, the day the drain was removed from the left upper quadrant stab wound, he began to exhibit a spiking temperature with peaks of 102 F (38.9 C). The fever was accompanied by headache, anorexia, left posterior thoracic discomfort, and left shoulder pain. Drainage of a small stitch abscess revealed Aerobacter aerogenes on culture. Three blood cultures were sterile; throat and sputum cultures contained no pathogens; and a urine culture grew out Proteus vulgaris, although the urinalysis showed neither pyuria nor albuminuria. A chest x-ray (fig. 1) showed fluid at the left lung base, although the possibility of underlying parenchymal disease could not be excluded. He was treated with oxytetracycline (Terramycin), 1 Gm. per day for four days, for possible pneumonia, but without improvement.

A medical consultation was requested on Oct. 18. A thoracentesis performed then was productive of 750 cc. of clear yellow fluid, with the characteristics of a transudate. In addition, the patient had moderate left upper quadrant tenderness and guarding, and a small amount of purulence was observed at the former drainage site. A post-thoracentesis x-ray showed elevation of the left hemidiaphragm, which had a somewhat ragged contour, absence of parenchymal lung disease, and disk atelectasis at the

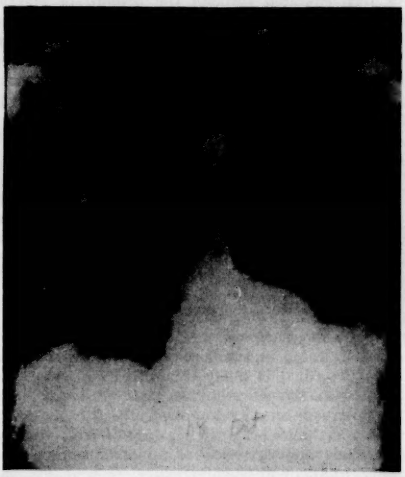

Fig. 1.—Initial roentgenogram of chest, showing pleural effusion at left base somewhat obscuring elevated left hemidiaphragm.

left base. It was felt that a left subphrenic collection or abscess was likely, and roentgenologic consultation was requested. Fluoroscopy disclosed an immobile, elevated left hemidiaphragm. Air was introduced into the stomach by the administration of a carbonated beverage and an impression was noted on the superior lateral aspect of the stomach bubble, along with medial and inferior displacement of the stomach remnant by a subphrenic mass (fig. 2).

It was decided to institute intensive antibiotic therapy, and the patient was treated with 20 million

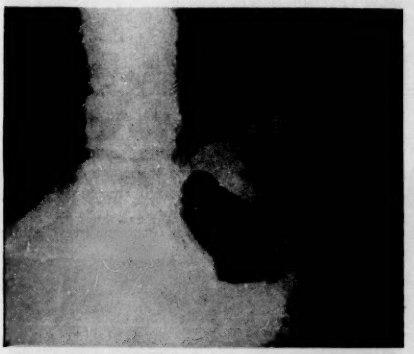

Fig. 2.—Roentgenogram of abdomen, showing superolateral impression on stomach bubble by left subdiaphragmatic mass. Displacement inferiorly and somewhat medially can also be seen.

units of penicillin intravenously during each 24-hour period and 0.5 Gm. of streptomycin intramuscularly twice a day. By Oct. 20, two days after the commencement of the intensive antibiotic therapy, the patient had become afebrile and asymptomatic except for minimal, left-sided, posterior thoracic discomfort and mild left upper quadrant tenderness. When the patient's temperature rose to 101 F (38.3 C) on Oct. 24, with concomitant increase in left upper quadrant tenderness, laparotomy was performed, with drainage of a left subphrenic abscess. Culture of the pus revealed hemolytic Staphylococcus aureus initially sensitive to all antibiotics, but a second culture and sensitivity test of the drainage on Oct. 28 revealed the organism to be insensitive to all antibiotics except chloramphenicol and erythromycin. He was treated with the former drug and made an uneventful recovery. Repeat examination of the stomach remnant on Jan. 12, with use of the same radiologic techniques as were previously used to demonstrate the abscess, showed complete resolution of the previously described changes (fig. 3).

Clinical and Diagnostic Picture

Although left-sided subphrenic abscesses due to suppuration in the left lung base and even the pelvis have been reported, the most frequent clini-

cal picture is one of prior upper abdominal surgery with lesions of the stomach, duodenum, and occasionally biliary tree predominating.[4] In a small number of cases there may be a relatively acute onset of symptoms 10 days to three weeks after surgery, but in most the onset is so insidious that the diagnosis may not be suspected for many weeks or months.[2]

Usually, but not invariably, fever and leukocytosis are present, along with signs of generalized toxicity such as chills, diaphoresis, anorexia, weakness, malaise, and weight loss. This is perhaps the signal for the clinician to recall Carter's modification of the old adage: "Pus somewhere, pus nowhere, pus not under the right diaphragm, pus under the left diaphragm."[5]

A variety of signs and symptoms referable to the thorax, the abdomen, or both may be present. Cough may occur, due to compression or basal collapse of the lung, and hiccough, due to diaphragmatic irritation.[6] Pain in the lower part of the chest and along the costal margin is often manifest, while

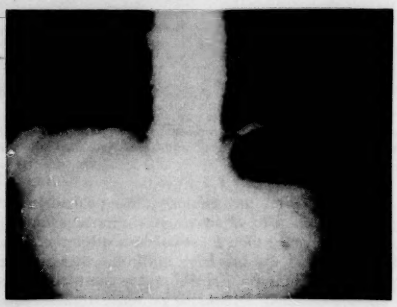

Fig. 3.—Roentgenogram taken three months after operation. Stomach bubble is in normal anatomic position.

authors differ markedly concerning the frequency of pain referred to the left shoulder and neck.[7] Abdominal pain and gastrointestinal symptoms such as vomiting, although frequent, are less common. A valuable clue is a local fulness of the chest, with a loss of elasticity of the chest wall and obliteration of the intercostal spaces. Of importance among the early findings is a point of tenderness on the chest wall where the abscess is most superficial, or, quite as significant but more often overlooked, an area of localized edema; either may not only reveal the diagnosis but provide the best localizing sign short of actual pus on aspiration.[3] Upper abdominal tenderness is a less useful sign, particularly soon after a gastrectomy.

Of vital significance is the presence of pleural effusion over the left diaphragm, and, less provocative, basilar atelectasis.[5] Neuhof and Schlossmann[2] reported "a pleural or pulmonopleural inflammatory process" in 78% of their cases, and a thoracoabdominal complex of signs in 31%. The discovery of a pleural effusion after abdominal surgery should immediately alert the clinician to the likelihood of a subphrenic abscess. A grievously frequent error has been to attribute such a sympathetic effusion to postoperative pneumonia, which rarely causes a pleural effusion and is almost inevitably accompanied by abundant sputum production from a purulent bronchitis. Before antibiotics the clear sympathetic effusion would become an infected empyema, but today the fluid remains clear, except in neglected cases; but a subphrenic abscess should at least be suspected in any empyema which does not clearly originate in the lung.[3]

A difference of opinion exists as to the advisability of exploratory aspiration for pus by introducing a needle through the diaphragm. In Neuhof and Schlossmann's series[2] pus was obtained by this means in 14 of 17 puzzling cases, and they strongly endorsed this procedure, with the needle left in situ as a guide to operation; they cautioned against false security derived from a negative result of aspiration, since the needle may be too short to reach a mediosplenic abscess under the central point of the diaphragm. Others, including Ochsner and De Bakey,[1] Rabin,[3] and Harley,[8] interdict this procedure, warning of the possibilities of perforation of a viscus or pleural contamination. Rabin[3] further advised care in decisions concerning the origin of pus aspirated through the seventh or eighth interspace, since infrapulmonary empyema is easily confused with a subphrenic abscess. He stressed the importance of a recent tooth extraction or unconsciousness in the differential diagnosis, attributing most infrapulmonary empyemas to perforated lung abscesses.

To further confuse the clinical picture Hochberg[9] emphasized that 5% of his 139 cases had fever, chills, and costovertebral angle pain and tenderness, and Beach and Tynan[6a] were concerned about the occasional difficulty of differentiation between a perinephric abscess and a subphrenic abscess with concomitant perinephritis. Of paramount importance, then, is the radiologic evidence.

Roentgenologic Aspects

The roentgenologic changes generally encountered in cases of subdiaphragmatic abscess have been described in many exhaustive and extensive reports on this subject. The case presented here offers an opportunity to review these changes as well as to describe a modification of technique in the study and detection of left-sided subphrenic abscess. Adequate roentgenologic examination, of course, is necessary in any suspected case of subphrenic disease, but the types of study and the findings will vary with the side of involvement and the extent of this involvement. Because of the difference of the anatomy of the right and left sub-

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phrenic spaces the roentgenologic findings in disease of these areas will differ. On the right the space and the spread of an abscess is limited inferiorly by the liver. Therefore, manifestation of disease on this side will affect the right diaphragm and the thorax more readily than will disease on the left, where the space is bounded inferiorly by the spleen, stomach, colon, and left lobe of liver—organs that can easily be displaced and moved. Consequently, abscess on this side, although it will affect the diaphragm and thorax, will also displace and affect the organs of the left upper quadrant, thereby giving the investigator a further chance to evaluate this area and make the diagnosis.

The routine roentgenogram of the chest frequently gives the first indication of disease under the diaphragm. Pleural effusion, considerable in amount or possibly minimal, occurs in the majority of cases of subphrenic abscess.[10] To detect small pleural effusion a roentgenogram made with the patient in the decubitus position with the involved side down is frequently valuable.

Fixation of the affected diaphragmatic leaflet in an elevated position is the most common and important roentgenologic sign of subphrenic disease.[11] This was found to be present in over 80% of Ochsner and De Bakey's cases. If a lateral film is obtained, localized flattening and elevation of the normal diaphragmatic contour, usually posteriorly, can also be frequently seen.[12] It has been noted that elevation of the diaphragm is more common in right-sided lesions and often not seen in those on the left because of previously mentioned anatomic differences.[13] Fixation of the diaphragm will occur in left-sided lesions, not infrequently, even without elevation.[5] Moreover, Neuhof and Schlossmann [2] state that neither diaphragmatic elevation nor fixation was present in 40% of their series of patients with left-sided subphrenic abscesses, while these diaphragmatic changes are rarely absent on the right.[14]

It must be remembered, however, that while an elevated, fixed diaphragm is characteristic and suggestive of subphrenic disease, other conditions may produce similar findings. For example, the most common and important of these is splinting of the diaphragm with a relative decrease in excursions secondary to recent surgery in the involved area. This is especially true of surgery of the right upper quadrant.[10]

The lung tissue above the elevated diaphragm is somewhat compressed, leading to disk atelectasis, which, when seen, should always suggest disease below the diaphragm. Occasionally, but much more rarely, more extensive atelectasis or even pneumonitis occurs in the basilar segments of the adjacent lung. The extensive roentgenologic changes which are seen with the more severe thoracic complications are beyond the scope of this discussion.[15]

Much has been written on the value of free air, or an air-fluid level, under the affected diaphragm in diagnosing this condition. There is no more definite roentgenologic sign than this when it occurs; however, the frequency reported in the literature varies, the figure most often quoted being about 25%.[16] The incidence appears to be much lower, however, in left-sided abscesses, and it is more likely to be missed on this side because gas from the stomach and colon obscures the area.[3] The air apparently originates from perforation of a viscus and not from anaerobic bacterial growth, as was previously considered. Air may be present under the diaphragm two or three weeks after abdominal surgery, and this must be kept in mind when a diagnosis of subphrenic abscess is made on the basis of this sign.[5]

Left-sided subphrenic abscess can be further delineated by keeping in mind the anatomic relation of the stomach to the subdiaphragmatic space. It has been suggested that when barium is placed in the stomach, displacement by a left subphrenic inflammatory mass can be demonstrated. Carter [5] and Friedman [10] advise that after ingestion of barium the patient be placed in the Trendelenburg position; the fundus of the stomach will normally be against the inferior diaphragmatic surface. However, if an abscess is present the stomach may be displaced inferiorly or possibly medially or anteriorly. Neuhof and Schlossmann [2] describe filling the stomach with air, by means of Seidlitz powder, and thereby visualizing the density of the abscess through the lucency of the gastric air bubble. These authors also described the anterior displacement of the stomach bubble by an abscess mass.

In the present case the patient was given a carbonated beverage to drink, and when he was in the upright position the air bubble was seen to be inferiorly placed; but, more important, an actual impression on the lateral superior aspect of the stomach bubble was produced (fig. 2). A similar study was performed on this patient three months after drainage of a left-sided subphrenic abscess, and the stomach bubble was then seen to be in its normal position with no residual impression (fig. 3). A review of the literature fails to reveal a similar published experience, although controversy exists as to the significance of indentation versus displacement of the barium-filled stomach in left-sided subphrenic masses.[2]

We believe that air is superior to barium as a contrast medium in the stomach in the study of left-sided subphrenic abscess, because it is much lighter than barium and therefore the stomach wall can be indented more easily, allowing a small abscess to be seen more readily. Also, air will expand the fundus of the stomach to a greater extent than barium and therefore has a greater chance of coming in contact with a subphrenic collection. In case of a perforation it is much safer to administer air and fluid than barium. The advantage of using air

becomes even more obvious if an intestinal perforation is suspected and the patient is receiving nothing by mouth; the examination for subphrenic abscess can still be performed by passing a nasogastric tube into the stomach and administering approximately 120 cc. of air in this way. After the appropriate films are taken the air can easily be withdrawn.

Finally, other procedures, such as diagnostic pneumoperitoneum and kymography, have been employed but found to be of limited use.

Comment

Probably the most important factor in the diagnosis of left-sided subphrenic abscess is the clinician's readiness to consider the diagnosis. The case reported here illustrates that a left-sided subphrenic abscess could and did develop despite routine postoperative antibiotic therapy, which may actually mask the situation and so demand greater alertness to the possibility on the part of the clinician. A clinical picture consistent with suppuration, within a variable length of time after upper abdominal surgery, should automatically suggest the possibility of a diagnosis of left-sided subphrenic abscess; the presence of a pleural effusion, or, less frequently, a thoracoabdominal complex should spur the clinician to attempt demonstration of the abscess by radiologic techniques. In this regard, it is the belief of the authors that the use of air to inflate the stomach or stomach remnant will greatly assist in delineating the abscess, particularly while it is still small. It is then, when the patient has not yet been debilitated by a lengthy battle against a chronic suppurative process nor as yet suffered a grave complication, such as rupture of the abscess into a viscus or the thorax, that he is more likely to respond to treatment.

The advice of Zaslow and Sachs [17] concerning treatment of the abscess with antibiotics appears judicious. These authors reported the cure of subphrenic abscess with intravenous therapy with oxytetracycline and quoted Maingot's recommendation that conservative treatment be attempted for three to six days, drawing on Crile's [18] extensive experience with penicillin treatment of intraabdominal abscesses. They proposed such therapy only so long as improvement continues and recommended instituting immediate surgical drainage at the cessation of resolution or the first sign of deterioration. In such a case, they believed, intensive antibiotic therapy at least promotes localization of the abscess and makes the patient a better operative risk. Just such a plan was followed in the case reported here, with striking improvement after the administration of massive doses of penicillin intravenously but subsequent deterioration, necessitating surgical drainage.

Concerning the proposal of Beach and Tynan [6a] that the clinician "cling and wait" for the abscess to point, because of possible confusion with a perinephric abscess, perusal of the literature caused us to feel that all too often the abscess might "point" into a viscus or the thorax. If roentgenologic techniques, including the one described in this paper, cannot further illuminate the situation, the exceedingly small number of cases of perinephric abscess that may be confused with subphrenic abscess [2] still do not justify accepting the risk of a perforation imposed by waiting, even with protective antibiotics.

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REEVALUATION OF MODERN ANTIBACTERIAL AGENTS USED FOR PERIRENAL ABSCESS

John J. Murphy, M.D.
and
F. Peter Kohler, M.D., Philadelphia

Diagnostic criteria, clinical course, and therapeutic results in cases of perirenal abscess were studied in 12 patients hospitalized with that diagnosis in the years 1937-1942. The data were compared with those from a similar group of 13 patients hospitalized in the years 1952-1958. The pattern of renal infections has changed in recent years. The later group of patients were older, were less acutely sick on admission, and had to be hospitalized longer. Their course was exemplified by that of a 52-year-old woman with a long history of calculi and other urologic troubles; these had culminated in marked fever and paralytic ileus after a retrograde pyelogram was taken, when contrast medium extravasated into a large perirenal cavity. Recovery followed incision and drainage of the perirenal abscess. The authors consider this the treatment of choice for perirenal abscess and conclude that antibacterial agents are ineffective in chronic parenchymal renal disease.

Infection of the renal parenchyma is the usual cause of perirenal abscess. Rupture of an abscess in the cortex of the kidney into the surrounding fat, with formation of a secondary collection in the space confined by Gerota's fascia, is thought to be the usual course of events. Infection anywhere in the body which causes bacteremia may lead to a cortical renal abscess and eventually to perirenal involvement. Primary infections in certain organs are frequent sources of renal cortical abscesses. Among these are dental and tonsillar abscesses, furuncles of the skin, and acute prostatitis. Within the kidney, pyonephrosis, nephrolithiasis, posttraumatic infection, and renal tuberculosis are common causes. Before the era of modern antibacterial agents, hemolytic Staphylococcus aureus was the offending organism in 80% of reported cases. Other organisms cultured were hemolytic streptococcus, Escherichia coli, Pseudomonas, Aerobacter aerogenes, and Proteus.

Reviews on perirenal abscess by Nesbit and Dick,[1] Hammer,[2] Campbell,[3] and Atcheson [4] stress the severely febrile course of the patient prior to drainage, with chills, marked tenderness and pain in the affected flank, and the usual absence or paucity of urinary symptoms or findings. Nesbit emphasizes that routine urine examinations may show completely normal findings in the presence of staphylococcic urinary tract infections and that staining of the urinary sediment is necessary to reveal the presence of the bacteria. The illnesses reviewed were usually of short duration and accompanied by a marked leukocytosis and slight anemia.

Aids in the diagnosis of perirenal abscess have been described by Beer [5] and Lipsett,[6] who emphasized characteristic roentgenographic findings such as absence of the psoas shadow on the affected side and elevation of the diaphragm. Others describe fixation of the kidney [7] and scoliosis of the vertebral column with the concavity of the curvature toward the involved side.[8] Retrograde pyelograms may indicate the presence of a perirenal abscess by demonstrating contrast medium in the perirenal space which communicates with the renal pelvis.[9]

Prior to the advent of effective antibacterial therapy, patients who developed a perirenal abscess were treated by incision and drainage as soon as the diagnosis was made. The literature preceding the development of modern antibacterial agents stresses the importance of early diagnosis of this condition and the necessity for immediate drainage in order to effect a cure and avoid complications. Failure to drain the abscess early often results in spread of infection to neighboring tissues. Nesbit and Dick [1] reported 16.5% pulmonary complications in 85 perirenal abscesses with six perinephrobronchial fistulas. Kuester [10] reported that 34 of 230 abscesses ruptured into the peritoneal cavity. Often the purulent material dissects along the psoas muscle of the involved side to point in the inguinal canal.

Incision and drainage of the abscess was acknowledged to be the proper therapy, and Campbell [3] states that a patient rarely recovered without operation. Even with drainage, the mortality was 24.5%, according to Hunt,[11] with 6.6% of deaths occurring immediately postoperatively and 17.9% within five years after operation.

From the Harrison Department of Surgical Research, Schools of Medicine, University of Pennsylvania, and the Department of Surgery, Division of Urology of the Hospital of the University of Pennsylvania.

The addition of potent antibacterial agents to the physician's armamentarium was accompanied by excessive optimism regarding the eradication of this bacterial infection. Occasional enthusiastic reports [12] appeared in the literature about the successful treatment of renal carbuncles and renal for a long time, with suppression of their acute septic episodes in part but with gradual decline of their general physical condition. In each patient, drainage of the collection of purulent material resulted in a restoration of general well-being and health.

TABLE 1.—*Salient Features of Twelve Patients with Perirenal Abscess*

Patient No.	Age, Yr.	Sex	Length of Illness Prior to Admission	Temperature at Admission, F	Hemoglobin Level, % of Normal*	White Blood Cell Count at Admission, per Cu. Mm.	Blood Urea Nitrogen Level, Mg.%	Organism in Abscess	Organism in Urine
1†	37	F	2 wk.‡	103.0	60	13,000	60	Aerobacter	Aerobacter
2	19	M	2 wk.§	102.0	74	27,600	9	Hemolytic Staph. aureus	.....
3	27	M	2 wk.‖	102.8	37	21,000	16	Hemolytic streptococcus	Proteus
4	28	F	1 mo.	101.8	73	17,900	11	Nonhemolytic Staph. aureus, Esch. coli, Aerobacter	.....
5	29	M	2 da.	103.0	92	19,700	15	Proteus	Proteus
6	34	F	6 hr.	105.0	70	11,000	10	Esch. coli	Esch. coli
7	24	M	5 da.	103.0	60	16,000	19	Hemolytic Staph. aureus	Hemolytic Staph. aureus
8	22	M	6 wk.	104.0	79	26,700	15	Hemolytic Staph. aureus	None
9	32	M	4 wk.	103.0	80	18,000	15	Hemolytic Staph. aureus	Hemolytic Staph. aureus, Esch. coli
10	44	M	10 da.	102.0	60	28,000	54	Nonhemolytic Staph. aureus	Nonhemolytic Staph. aureus
11	22	M	3 wk.	102.0	70	18,000	15	Hemolytic Staph. aureus	.....
12	39	M	2 wk.	102.0	43	11,800	23	Hemolytic Staph. aureus, Esch. coli	Esch. coli
Av.	30	..	2.3 wk.	102.8	66	19,060	22	.....	.....

* Normal = 14 Gm.%.
† Died.
‡ Tooth extraction, backache.
§ Pain in upper right quadrant.
‖ Pain in left flank.

TABLE 2.—*Characteristics of Disease in*

Patient No.	Age, Yr.	Sex	Length of Illness Prior to Admission	Temperature at Admission, F	Hemoglobin Level, Gm.%	White Blood Cell Count at Admission, per Cu. Mm.	Blood Urea Nitrogen Level, Mg.%	Organism in Abscess	Organism in Urine
13	45	F	2 mo.	100.4	10.5	12,400	15	Aerobacter, Pseudomonas	Aerobacter, Pseudomonas
14	51	F	8 wk.	101.0	4.2	14,300	12	Aerobacter	Aerobacter
15	35	M	6 wk.	100.0	5.6	14,000	49	Proteus, Aerobacter	Proteus
16	46	F	1 wk.	104.0	11.36	26,800	32	Esch. coli Pseudomonas, Proteus	Proteus
17	45	F	3 wk.	99.0	9.5	14,900	29	Paracolon, Proteus	Proteus
18	7	F	10 da.	101.0	8.7	8,900	21	Proteus, Esch. coli	Proteus
19*	26	F	6 mo.	102.0	5.4	22,300	86	Proteus, Esch. coli	Proteus
20	65	M	3 wk.	100.0	14.1	7,700	14	Proteus	Proteus
21	65	M	5 mo.	99.0	10.7	10,300	16	Nonhemolytic streptococcus, 7,300 cc. fluid in abscess cavity	No growth
22	58	M	9 wk.	98.0	7.4	9,800	33	Esch. coli, 600 cc. fluid in abscess cavity	No growth
23	53	F	2 mo.	100.8	6.1	9,200	14	Proteus, 700 cc. in abscess cavity	Proteus
24	52	F	7 mo.	100.8	7.4	6,000	43	Aerobacter, 3,000 cc. fluid in abscess cavity	Pseudomonas
25	60	M	1 yr.	99.4	5.9	5,000	22	Proteus, 300 cc. fluid in abscess cavity	Proteus
Av.	47	..	13 wk.	100.5	8.2	12,400	30		

* Died.

cortical abscesses by means of these agents. It soon became evident [13] that the antibacterial drugs did not always eradicate the infection but often masked the true signs and symptoms of the disease process.

Recently, within a short time interval, several gravely ill patients with perirenal abscesses were admitted to the University Hospital. These persons had been treated with antibacterial agents

In order to determine the effect of modern antibacterial therapy on the treatment of perirenal abscesses, a survey was made of the experience with this lesion in the University Hospital in the era preceding the antibacterial agents and in a recent similar period of time. Table 1 lists the salient features of 12 patients admitted to the University Hospital with a diagnosis of perirenal abscess between July, 1937, and October, 1942.

Most of these patients were in the second and third decade of life and were admitted to the hospital with a relatively short history of illness and with a high fever. Leukocytosis was marked and anemia rare. In 8 of the 12 patients the offending organism was a hemolytic Staphylococcus aureus.

Related Infection	Lithiasis	Admission Date	Discharge Date
Pelvic inflammatory disease, chronic pyelonephritis	None	7/26/37	8/24/37
Sinusitis since 1935	None	12/21/37	1/21/38
Periurethral abscess, stricture for 5 mo.	None	12/23/37	1/30/38
.....	Ureteral stone	1/23/38	2/ 4/38
Pyelolithotomy June, 1939	Previous renal calculus	8/12/39	8/31/39
Urinary tract, 4 yr.	Renal calculus on right, 4 yr.	5/ 6/39	6/27/39
Urinary tract	Pyelolithotomy on right, calculus	8/18/40	8/29/40
Sore throat	.....	12/ 4/39	1/ 1/40
.....	.....	4/21/41	5/19/41
Urinary tract	Bilateral calculus since 1933	1/14/42	3/28/42
Upper respiratory tract	None	5/ 9/42	6/ 8/42
Pyelolithiasis, 13 yr. ago	Bilateral renal calculus	10/31/42	11/29/42
.....	.....	....	....

Thirteen Patients with Perirenal Abscess

Related Infection	Lithiasis	Antibiotic Given	Admission Date	Discharge Date
Nephrolithotomy on right in 1950, on left in 1949	Bilateral	Penicillin, 300,000 units b.i.d.; sulfadiazine, 0.5 Gm. q.i.d.; streptomycin, 0.5 Gm. q.i.d.; 1 mo.	8/18/52	8/27/52
Nephrolithotomy, 1950	Bilateral	Penicillin, 300,000 units t.i.d.; streptomycin, 0.5 Gm. b.i.d.; 6 wk.	3/16/52	3/16/52
Urinary tract	Bilateral	Penicillin, 300,000 units t.i.d.; sulfadiazine, 0.5 Gm. q.i.d.	7/26/54	8/21/54
Urinary tract	Bilateral	Penicillin, 300,000 units, q.i.d., 3 days	12/29/54	1/23/55
Urinary tract	Bilateral	Chloramphenicol, 250 Gm. q.i.d., 3 wk.	2/24/55	3/ 5/55
Urinary tract	Bilateral	Penicillin: streptomycin; sulfisoxazole; and chloramphenicol; since 1948	9/10/55	9/10/55
Chronic pyelonephritis	None	.....	10/ 2/55	10/ 2/55
Chronic pyelonephritis	Pyelolithotomy 1944, calculus 1955	Chloramphenicol, 250 Gm. q.i.d., 1 wk.	2/ 2/58	2/11/58
Urinary tract	Right renal pelvis since age 18	Penicillin: streptomycin; 5 mo.	7/15/58	8/ 4/58
Urinary tract	Bilateral since 1956	Penicillin: chloramphenicol: sulfisoxazole: 9 wk.	9/16/58	10/ 5/58
Urinary tract	Right renal & ureteral calculus	Chloramphenicol, 250 Gm. q.i.d.; nitrofurantoin, 100 Gm. q.i.d., 2 mo.	9/29/58	10/22/58
Urinary tract	Right renal calculus	Chloramphenicol, 10 wk.; polymyxin: kanamycin	10/23/58	11/15/58
Chronic pyelonephritis	None	Chloramphenicol: nitrofurantoin; sulfisoxazole; 3 mo.	10/30/58	12/ 9/58

Fifty per cent of the patients had concomitant renal calculi or other urinary tract disease. Eleven patients recovered after incision and drainage of the abscess.

Table 2 demonstrates some significant changes in the disease picture as demonstrated by 13 patients admitted to the University Hospital with the diagnosis of perirenal abscess between August, 1952, and October, 1958. These patients were older, the average age being 47 years. The majority had renal calculi and all had a history of urinary tract infection without a history of a distant focus of infection. This may indicate that the antibacterial agents are effective in preventing the spread of bacteria from infections such as sinusitis and tonsillitis to the kidney parenchyma. It would also appear that, in cases of long-standing renal infections, especially when calculi are present, the antibacterial agents are ineffective in preventing spread of the abscess and in reaching and eradicating the central focus. Most of the patients had low-grade fever, and some were afebrile at the time of admission. Leukocytosis was not as marked as in the patients listed in table 1, and moderate to severe anemia was usually found. All had been ill for long periods of time, the shortest period being one week and the longest one year, with an average duration of illness of 13 weeks prior to admission. Staphylococci were only occasionally encountered, whereas Proteus and coliform organisms seemed to predominate. Despite the fact that almost all of the patients had been given two or more supposedly potent antibacterial agents, the infections persisted and produced weight loss, cachexia, and anemia.

The course of one of the patients in the most recent series was thought to merit a detailed description because it clearly demonstrates the extent to which antibacterial agents may mask the clinical picture and hinder a patient's recovery from what should be an acute and brief illness.

Report of a Case

A 52-year-old female had an attack of renal colic in 1947. At that time, she passed a calculus, presumably from the right upper part of the urinary tract. An intravenous urogram after the attack was reported to be normal. In 1950, she had another attack of pain in the right flank and hematuria and again passed several calculi. She remained asymptomatic until January, 1958, when she was

treated for anorexia, fatigue, and weight loss. She had pyuria but no other definitive symptoms until Feb. 14, when she had an episode of hematuria.

An intravenous pyelogram at that time revealed poor function on the right side, and a retrograde pyelogram on Feb. 18 (fig. 1 and 2) revealed

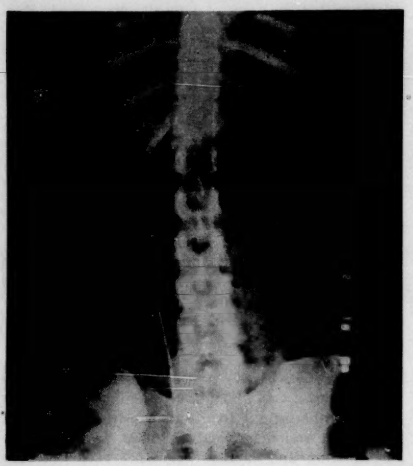

Fig. 1.—Ureteral catheter shown in place. Two calculi are seen within right renal shadow. Note normal right psoas shadow.

extravasation of the contrast medium from the upper calyx into an irregular cavity which appeared to extend beyond the parenchymal shadow. Two small calculi were seen on the right below the diaphragm in close proximity to this cavity. After the retrograde pyelogram had been made, the patient became extremely ill with marked fever and a paralytic ileus. The blood urea nitrogen level rose to 52 mg.%. Aerobacter aerogenes was found in the urine culture. The patient was treated with chloramphenicol and prednisone (Meticorten) and general supportive therapy. She slowly recovered and was discharged from the hospital on March 30, 1958. Therapy with antibiotics was continued, but her symptoms of anorexia, weight loss, and fatigue persisted and she had to be readmitted July 18, 1958. Early in September, 1958, the antibacterial therapy was discontinued and the patient immediately experienced febrile episodes with a temperature of 102 F (38.9 C) every evening. She also developed gradually increasing pain in the right flank and was readmitted to the hospital on Oct. 10, 1958, with nausea, vomiting, and diarrhea. Chills and fever persisted despite administration of antibacterial agents, and she was transferred to the University Hospital on Oct. 23.

At the time of admission, the patient had constant pain in the right flank. She had lost 40 lb. (18 kg.) in the four months preceding admission and was in a state of extreme weakness and exhaustion. There was bilateral pitting ankle edema. She had some dyspnea, and a temperature of 100 F (37.8 C) each evening. At the time of her admission, the blood pressure was 96/66 mm. Hg and the pulse 108 per minute. She was pale and weak. A large fixed and tender mass filled the right side of the abdomen. A roentgenogram of the chest revealed a markedly elevated right side of the diaphragm (fig. 3). Despite supportive therapy, the patient's general condition was slow to improve and the blood urea nitrogen level increased daily. It was felt that the expanding abscess was interfering with drainage from the right kidney. The hemoglobin level was 7.4 Gm.%; the white blood cell count was 6,000 per cubic millimeter, with 72% neutrophils, 24% lymphocytes, and 4% eosinophils. The blood urea nitrogen level was 43 mg.%.

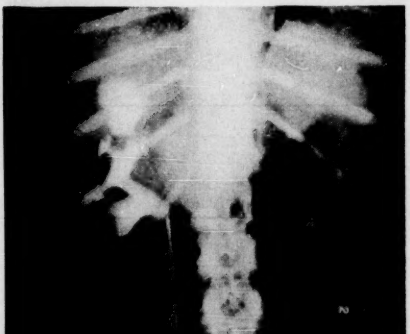

Fig. 2.—Retrograde pyelogram showing extravasation of contrast medium into perirenal area.

Urinalysis revealed a specific gravity of 1.010, 2+ protein, and no sugar. The specimen was loaded with white blood cells and bacteria. Urine culture revealed Pseudomonas. The patient was given a transfusion with whole blood until the hemoglobin level was 12 Gm.%.

Incision and drainage of the abscess in the right retroperitoneal space was carried out on Nov. 4.

Three thousand cubic centimeters of thick white pus was removed and the cavity drained. Aerobacter aerogenes was isolated from the purulent material. The postoperative course was marked by constant improvement in the patient's appearance and strength. She was discharged on Nov. 15.

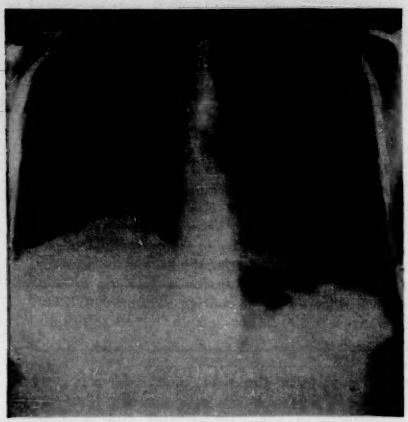

Fig. 3.—Roentgenogram showing elevation of right side of diaphragm.

Summary and Conclusions

The clinical course of patients with perirenal abscess treated before and after the advent of modern antibacterial agents has been compared. It appears likely that these agents have controlled some of the more common sources of renal infection, such as tonsillitis and furunculosis, since the patients in the more recent series were older and almost invariably had serious intrarenal disease. At the same time, it is apparent that the antibacterial agents are ineffective in eradicating chronic parenchymal renal disease. This treatment may mask the symptoms produced by perirenal abscess so that the correct diagnosis is not made. Extreme clinical deterioration of the patient may result. It is apparent that incision and drainage remains the treatment of choice in this disease process.

3400 Spruce St. (4) (Dr. Murphy).

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THYROIDITIS.—The two types of thyroiditis most frequently encountered are subacute thyroiditis and Hashimoto's disease. Subacute thyroiditis is a self-limited disease of unknown etiology, characterized by a tender gland with a diminished I^{131} uptake in the acute phase. Although there is no cure, adrenal steroids and x-ray treatment offer good symptomatic relief. Hashimoto's disease is a distinct and increasingly common clinical entity which must be differentiated from other types of nodular goiter. This can usually be done by finding a rubbery, diffusely enlarged gland, a BMR below 0 per cent, and a normal to high I^{131} uptake. Patients with Hashimoto's disease will have myxedema or will eventually develop it, and the proper treatment is desiccated thyroid. . . . Very little need be said regarding Riedel's type of invasive fibrous thyroiditis, since most physicians will never see a case and, if they do, the proper preoperative diagnosis should be carcinoma.—J. B. Selby, M.D., The Diagnosis and Treatment of Thyroiditis, *The Journal of the Kentucky State Medical Association*, July, 1959.

PROBLEMS IN THE EVOLUTION OF OBSTETRICS

Nicholson J. Eastman, M.D., Baltimore

Obstetrics in the past has been concerned with such questions as the propriety of using anesthesia during labor and the desirability of using sutures to close the uterine wound after cesarean section. Obstetrics in the future will have to face equally fundamental questions. New knowledge is needed in order to solve the problems of premature birth, stillbirth, neonatal death, congenital malformations, and toxemia of pregnancy. Better utilization of existing knowledge is needed also, especially in training the personnel that will be required if adequate, individualized care is to be given to future obstetric patients, in view of the soaring birthrate.

We are commemorating the 100th anniversary of the founding of the Section on Obstetrics and Gynecology of the American Medical Association, which was established in 1859 under the name "Section on Practical Medicine and Obstetrics." Several circumstances serve to make this meeting of our Section a noteworthy occasion. Thus, it is an honor to welcome as our official guest the distinguished president of the Royal College of Obstetricians and Gynecologists.

As we celebrate this centennial, moreover, it may be permissible to note in passing that we are in the best company, for the year 1959 happens to be one rich in centennials. In the field of English literature, the year of 1859 saw the publication of Tennyson's "Idylls of the King," of Dickens' "Tale of Two Cities," and of Edward Fitzgerald's translation of "The Rubáiyát of Omar Khayyám." In January of the same year our own Dr. Oliver Wendell Holmes, of puerperal infection fame, began the publication of his "Professor at the Breakfast Table" in the *Atlantic Monthly*. In the sphere of biology, the year of 1859 witnessed the appearance of a volume which has probably had a more profound effect on modern scientific thought than any other single work—Darwin's "Origin of the Species." In an area nearer to our own, Florence Nightingale's "Thoughts on Nursing," published also in 1859, marked the beginning of a new epoch in patient care.

In the fields of literature, biology, and nursing, the year 1859 was an illustrious one. But what, in the same year, was taking place in obstetrics and gynecology? Alas, there was little that was good and much that was bad. Although Semmelweis had demonstrated the cause of puerperal infection 10 years previously, the widespread and vitriolic attacks which were being made on his theory, just 100 years ago, were too much for his sensitive nature and were responsible, as we all know, for his subsequent insanity and death. Likewise, Simpson's introduction of anesthesia into obstetrics had met with denunciation in many quarters, and by 1859 he was spending a goodly part of his time in rebutting the attacks of the many who maintained, on Biblical grounds, that it was sinful so to interfere with natural childbirth, a theme which recalls to mind a certain present-day altercation. Many dedicated physicians of that period, it is true, were devoting their best energies to the improvement of obstetrics; but for the most part, maternity care was in the unclean hands of a vast horde of untrained, ignorant, superstitious, and often alcoholic old women; it was a clandestine and lowly trade rather than a profession.

From the Department of Obstetrics, the Johns Hopkins University School of Medicine and Hospital.

Chairman's address, read before the Section on Obstetrics and Gynecology at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 10, 1959.

Early Development of Cesarean Section

To recite the many lifesaving advances which have elevated obstetrics from its low level in 1859 to its present status in 1959 would be to recount a series of events well known to everyone in our specialty, and to review them now would seem unnecessary. But since this is the American Medical Association and since we celebrate today the action taken by certain American worthies in 1859, it would seem appropriate to dwell briefly on the greatest single contribution which has been made by American physicians to obstetrics over the past 100 years. I refer to the well-nigh forgotten role of frontier America in the early development of cesarean section.

Throughout the greater part of the 19th century, cesarean section was the most fatal of surgical procedures. In Great Britain and Ireland, the maternal mortality from the operation had mounted in 1865 to the appalling figure of 85%. In Paris, during the 90 years ending in 1876, not a single successful cesarean section had been performed. The results in Germany, Austria, and Italy were so poor that the newly introduced operation of Porro, which included hysterectomy as well as hysterotomy, was superseding the old and almost universally fatal cesarean section.

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The turning point in the development of cesarean section was clear-cut and decisive. It was the appearance in 1882 of a monograph by Max Sänger, then a 28-year-old assistant of Credé in the University Clinic at Leipzig in which the routine employment of uterine sutures was recommended in cesarean section. Prior to Sänger's monograph, uterine sutures in cesarean section had been denounced in Europe as superfluous as well as harmful. In 1770 Andre Levret, the foremost obstetrician of 18th century Paris, had taught that uterine sutures in cesarean section "were not only prejudicial but were absolutely useless because of the prodigious contractions which the uterine muscle undergoes following delivery." Blundell, in his "Principles and Practice of Obstetric Medicine," published in 1840, dismissed the subject with the remark that "sutures to the uterus have not hitherto been in general employ."

Sänger deprecated the growing tendency to abandon the old classic cesarean section in favor of the new Porro procedure, since he believed that careful coaptation of the uterine wound with sutures would obviate all difficulties and permanently establish the superiority of the older operation. But whence came Sänger's idea? Certainly not from his own experience, because his monograph, although reciting *in extenso* the advantages of uterine sutures as he envisaged them, was actually based on only a single successful case in which he had tried them. Nor did it come from his colleagues in the sophisticated centers of Europe, for, as we have seen, sutures were not in favor there. It came, as Sänger very graciously and generously acknowledged, from frontier America, where surgeons working in the outposts of the newly developed Midwest had reported no less than 17 cesarean sections in which uterine sutures had been used. Eight mothers lived and nine died—an incredibly good record for those days. Sänger's monograph includes a table showing the details of these 17 operations. This table was the documentation of his contention and the basis of his monograph. Confirmation of Sänger's convictions in respect to uterine sutures in cesarean section followed quickly. Within a few years suture of the uterus was generally recognized as an indispensable part of cesarean section and the modern operation came into being.

But how did these American surgeons hit upon the idea of using sutures in cesarean section? The first of these operations was performed by a Kentucky surgeon, Frank E. Polin, in December, 1852; he used silver wire sutures, and most of the other 16 sections performed in the Midwest between 1867 and 1880 were done with silver wire sutures. It is significant that in the January preceding Polin's operation, there appeared the celebrated paper of the Alabama surgeon, J. Marion Sims, on the use of silver wire sutures in vesicovaginal fistula and, although Sims did not mention the use of silver wire in cesarean section, it appears that the general idea bore fruit at the hands of these frontier practitioners. By demonstrating the earliest successful type of uterine suture in cesarean section and by furnishing the supporting data for Sänger's monograph, these pioneers made a contribution of immeasurable importance to obstetrics, which we can look back on with pride.

Research Problems of the Future

Having looked back, let us also look forward and ask ourselves, "What are the major problems and challenges which obstetrics in the United States faces in the years to come?" In view of the dramatic reduction in maternal and perinatal mortality which has been achieved during the past few decades, it might seem off-hand that all is well with American obstetrics and that we can now rest on our oars. But all is not well with our obstetrics, and any glib self-satisfaction about its status not only is out of place but can do our specialty irreparable harm. In looking to the future our problems fall quite naturally under two headings: those concerned with the need for new knowledge and those concerned with the best utilization of existing knowledge.

Premature Birth.—In regard to the need for new knowledge, the transcendent problem in obstetrics, not only in the United States but throughout the world, is the cause and prevention of premature birth. More than half of all neonatal deaths are the result of premature birth. One-third of all cases of cerebral palsy are attributable to the same cause. Although some premature births can be explained on the grounds of known factors such as abruptio placentae, placenta previa, multiple pregnancy, and certain maternal complications which demand artificial termination of pregnancy, such as preeclampsia, about 60% of premature births occur without explanation. The importance of these unexplained premature deliveries lies not only in the toll they take in lives of newborn infants and in neuropsychiatric normalcy but in the circumstance that they represent in essence some defect in one of the basic phenomena of reproduction, uterine contractility; there is reason to suspect that this defect in turn stems from some even more basic disorder of the endocrine system. Whatever the cause of premature labor may be, its elucidation and prevention would be the greatest boon that the discipline of obstetrics could confer upon mankind.

Fetal Physiology.—The second most important research problem in obstetrics, as I see it, is fetal physiology and its derangements. This field encompasses, let it be noted, the science of genetics and all that the genes contribute to fetal normalcy or abnormalcy, both physical and mental. It includes

also, of course, the many-sided problem of fetal environment—the oxygen supply of the fetus, its nutritional needs, its immunological relationships to the mother, its acid-base balance, its enzyme systems, and many other environmental circumstances essential to fetal well-being. As we all know to our sorrow, any pronounced deviation from the normal in any of these factors may cause stillbirth, neonatal death, and congenital malformations; in sublethal degree it seems probable that they are responsible also for various types of neuropsychiatric disorders. This area is a fairyland for investigation and well worth a lifetime of research to any young man who approaches it with dedicated zeal coupled with working knowledge of a pertinent basic science.

Toxemias of Pregnancy.—As for that age-old enigma of obstetrics, the cause of the toxemias of pregnancy, I would rank it third in importance to the two problems just surveyed. Most maternal deaths from the toxemias today are the result of neglect, either self-neglect by the patient or negligence on the part of the doctor. The majority could be prevented by the timely application of existing knowledge. Preeclampsia per se is not a cause of premature labor but looms large in the over-all picture of prematurity because it often forces the obstetrician's hand to terminate a pregnancy prematurely. I am cognizant of other ways in which the toxemias may prove injurious to both maternal and fetal welfare, but in my opinion the elucidation of the first two problems mentioned would contribute more to human happiness and progress than further knowledge about the toxemias.

Individualized Care of Mothers

The three problems which we have just reviewed represent areas of obstetrics in which new knowledge is urgently needed. Let us turn now to the other phase of our inquiry, namely, how existing knowledge may best be utilized in the United States over the next decade. Here we face a crucial problem. Indeed, on its correct solution we stand or fall. The problem is this: How, with a diminishing personnel and a soaring birth rate, can we hope to give to the mothers of 1970 the meticulous, individualized care which they deserve?

In an article which appeared in the January, 1954, issue of *Children*, published by the Children's Bureau, I set forth this problem in detail with full documentary data, both in respect to the physician shortage which may be anticipated in the 1960's and in regard to the concomitant increase in births. During the intervening five years, the same problem, with new, confirmatory data, has been laid before the American Public Health Association and the American College of Obstetricians and Gynecologists by Dr. John Whitridge Jr. of our clinic. The problem has hence been adequately publicized and is doubtless familiar to you all. Accordingly, a bare statement of the essential facts of the issue will suffice for our present purposes.

The most recent and authoritative estimate of the number of births which will take place in the United States during 1970 is 6 million. This represents a 50% increase in the number of births over those in 1958, and let it be remembered, 1970 is less than 11 years off. Why is a sharp rise in births anticipated? In the mid-40's any overworked obstetrician could have warned his commissioner of public schools to expect a huge increase in first grade pupils around 1952, and exactly this happened. The same obstetrician, on the basis of the soaring birth rates in the 1940's, could have told university authorities to expect an enormous increase in students in the 1960's. On this problem, the Bayne-Jones consultants on medical education and research, in their final report to the Secretary of the Department of Health, Education, and Welfare, as of June, 1958, stated:

> By 1970, the college-age population will be 26 million. This represents nearly a 75 per cent increase above the present level of 15 million, as contrasted with more than a 10 per cent decline (almost 2 million in absolute terms) in this age bracket over the past decade. It should be emphasized that all persons included in this 1970 estimate are now in elementary school.
>
> Drawing from this vastly expanded population base and spurred by strong social and economic incentives, college enrollments will increase steadily and will probably reach 6.4 million by 1970 as contrasted with 3.4 million in 1957. The higher education system of the country clearly faces a decade or more of extreme stress.

Likewise, unless our country is stricken by some major and unprecedented calamity, the marriage bureaus of 1970 will confront a period of extreme stress, because students of college age are rapidly becoming young men and women of marriageable age. More marriages result in more babies. This is the basis for predicting that the volume of maternity work in this country will augment sharply in the 1960's and reach a 50% increase over the present amount by 1970.

Who is going to care for this stupendous number of births? As for medical personnel, all authoritative studies forecast for the 1960's a decrease in the number of physicians in relation to population. On this issue, the Bayne-Jones report makes the following statement:

> A minimum of 14 and as many as 20 new medical schools will have to be built if the existing number of physicians per 100,000 is not to fall. . . . Even if funds in the order of $500 million to $1 billion dollars were made available immediately for construction of new medical schools, it seems certain that the number of physicians per 100,000 population will decline between now and 1970.

This then is the problem—a 50% increase in births between now and 1970 and a diminishing number of physicians in relation to population. In

laying this issue before you, it is my main purpose to reiterate its urgency and to implore the several organizations devoted to our specialty to give it serious thought and take appropriate action. Two programs which might conceivably alleviate the shortage of obstetric personnel anticipated for the 1960's are as follows.

Group Practice.—The most practical and realistic way of meeting the problem—one that we know by experience will work—is more group practice. By this is meant the care of obstetric patients by a group of four or five obstetricians who work interchangeably as a unit. For example, on a given day, while obstetricians A and B are seeing antepartum and postpartum patients in the office and handling telephone calls throughout the whole day, obstetrician C is spending a full 24 hours in the delivery suite, managing labors and answering calls throughout the entire night, while obstetrician D is completely off duty for 24 hours. From the viewpoint of a well-ordered life, there would be no night calls whatsoever except for the man on 24-hour duty in the delivery suite; every fourth day each man would be entirely free. From the standpoint of good maternity care, the patients would be assured of the services of a wide awake and alert obstetrician who, when on delivery duty, would be able to give his undivided time to the needs of the parturients. From the viewpoint of the threatened paucity of personnel, four obstetricians in such group practice can handle perhaps eight times the number of cases which any one obstetrician could manage in solo practice. This means a doubling of work output for the group. Finally, there is good reason to believe that programs of this type would make obstetrics a more appealing specialty to our medical graduates.

As we all know, the chief objection to such group practice will come from many patients who insist on care throughout by their favorite obstetrician and by no one else. Although this objection will long be a hindrance to the development of such programs, it may be answered in two ways. 1. Group practice of the type described is not new but has worked successfully and to the complete satisfaction of patients in many localities. 2. Little by little, expectant mothers must be led to understand that any competent obstetrician who is wide awake and alert is a safer and more trustworthy man than the best obstetrican in the world who is harassed by overwork and groggy from lack of sleep.

Obstetric Assistants.—The work output of a group of obstetricians could be increased in both quantity and quality if they could have the round-the-clock assistance of a few graduate nurses who have received special training in the conduct of normal pregnancy, labor, and the puerperium. By training is meant not less than eight months' full-time clinical tutelage under the supervision, control, and accreditation of obstetricians. The best appellation for such auxiliary personnel would be "obstetric assistants." With proper training such nurses would be competent to perform, if need be, the following services: in antepartum care—history taking, blood pressure determinations, venipunctures, abdominal palpation, fetal heart observations, and attention to the more common complaints such as nausea, heartburn, constipation, and excessive weight gain; in labor—in addition to the procedures just mentioned, they would be available to carry out rectal examinations, emotional support of the parturient, and, if need be, nearly the entire conduct of labor except actual delivery. This would be undertaken only in an emergency, but they should be trained for this eventuality. If, at any time, the slightest abnormality developed, the obstetrician would be notified immediately. It must be emphasized that these obstetric assistants would at all times serve under the direct supervision and control of obstetricians, and always in hospitals or in doctors' offices.

The term "nurse midwife" is often applied to this type of personnel, which I have designated, by preference, as "obstetric assistants." Most nursing groups and organizations devoted to the development of these obstetric assistants much prefer the term "nurse midwife." Moreover, many nurses so trained choose to serve in underdeveloped countries and can be accredited by such international bodies as the World Health Organization only as "nurse midwives." For these two reasons this appellation is gaining currency despite the stigma which the word "midwife" carries in the United States. But, by whatever name they may be called, my own experience with these nurses indicates beyond question that they have much to contribute to maternity care in the United States and that, when the need exists, they can do a great deal to relieve overworked obstetricians of routine burdens.

But, as indicated, it is my purpose to pose this question of paucity of obstetric personnel in the 1960's rather than to answer it. It is an urgent problem, because personnel cannot be developed overnight. In addition, the need for more maternity beds requires investigation, because already, in most hospitals, the stay of maternity patients has been reduced to a shameful and irreducible minimum. If steps are not taken to meet these two problems, the problem of obstetric personnel and the problem of hospital facilities over the next decade, and if the mothers of 1970, just 11 years hence, are neglected because of inadequate personnel and shortage of maternity beds, their neglect tomorrow will be the direct result of our apathy and indecision today.

MANAGEMENT OF URETERAL INJURIES

William J. Staubitz, M.D., Imre V. Magoss, M.D., Melbourne H. Lent, M.D., Eugene M. Sigman, M.D.
and
Oscar J. Oberkircher, M.D., Buffalo

Ureteral injuries occurring in 22 patients during surgical and irradiation therapy of abdominal cancer were studied, with the intention of improving the management of this operative hazard. The most frequent type of damage was physical trauma from accidents of surgical technique: puncture, crushing, or ligation of the ureter. Fibrosis, secondary to radiation of tumors close to the ureters, occurred in three patients. A majority of the injuries were diagnosed and repaired at the time they occurred; this is the best plan of management. When an injury was not noticed, the signs and symptoms usually observed in the immediate postoperative period were pain, fever, azotemia, anuria, and urine draining from an abnormal site. A blood-free operative field and careful surgical dissection will keep accidents at a minimum, but if one does happen the surgeon must be prepared to repair the ureter, with varied techniques, depending on the site, type, and extent of the injury. Preoperatively an outline of the urinary tract should be obtained (by roentgenography) and indwelling ureteral catheters inserted if possible.

Injury to one or both ureters has been a hazard in surgery of the pelvic organs since surgeons first began operating in this area. These injuries have become more prevalent during the last few decades, since surgeons have adopted a more radical approach to therapy of malignant disease involving the pelvic organs and colon. This paper reports a study of the management of ureteral injuries occurring in an institution in which advanced malignant lesions are treated by both extensive surgery and irradiation.

The incidence of ureteral injuries as reported by different authors varies between 0.5 and 10%.[1] The exact incidence has never been established, because many of these surgical accidents may not be reported and also because unilateral injuries may remain asymptomatic and, consequently, may not be recognized.

We shall not attempt to establish a rate of ureteral injury in this study because, while complete pretherapy and post-therapy urologic evaluations are done routinely on all gynecologic patients, they are done only when requested on patients of other services. Therefore, it is possible that certain patients undergoing rectocolonic surgery may have suffered unilateral injuries which have not manifested themselves clinically.

Causes and Types of Injury

Abdominal and pelvic surgical procedures are regarded as the most frequent cause of ureteral injury. Anatomically, the ureters are well protected from external trauma; however, their proximity to the large intestine and pelvic viscera makes them vulnerable to surgical and radiologic trauma.

In the pathogenesis of these surgical accidents five factors appear significant: (1) control of hemorrhage after a slipped or broken ligature, with hasty attempts to reclamp the usually retracted bleeding vessel without direct vision; (2) removal of large tumors, when the size of the lesion itself or the operative manipulation may alter the normal anatomic landmarks; (3) interference with the blood supply, without direct injury to the ureter; (4) closure of the posterior peritoneum, with kinking or displacement of the ureters (subsequent healing and scarring may result in further obstruction, necrosis, and/or fistulas); and (5) needle punctures, necrosis from clamps, and the indiscriminate use of transfixion sutures without the benefit of direct vision.

Our series of 23 ureteral injuries occurred in 22 patients. The highest incidence of injury followed the Wertheim radical hysterectomy for carcinoma of the cervix. Among eight patients with nine ureteral injuries one patient suffered a bilateral injury and seven patients had unilateral involvement. The right ureter was injured in three instances and the left in six. Five injuries resulted from necrosis, the exact cause of which was never determined but was thought to be interference with the blood supply; three injuries were caused by transection and one by ligation of the ureter.

Surgery of rectocolonic lesions, both malignant and benign, accounted for five accidents to the ureter. Three injuries occurred during a Miles' abdominoperineal resection for tumor of the recto-

From Roswell Park Memorial Institute, and the Department of Urology, University of Buffalo School of Medicine.

Read before the Section on Urology at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 10, 1959.

sigmoid: two ureters were transected and one developed necrosis because of angulation. The fourth injury occurred when a ureter was transected during an anterior resection for carcinoma of the sigmoid colon and the fifth when a ureter was transected during surgery for diverticulitis of the descending colon.

Four injuries were caused by radiation therapy, both external and interstitial, for malignancy of the cervix and vagina. Specimens obtained from the sites of obstruction in these cases indicated fibrosis only.

The five remaining accidents occurred during pelvic surgery for lesions of the female genital tract. In one case a left ureter was ligated during removal of a large granulosa cell tumor of the ovary. Four injuries occurred during hysterectomy for benign lesions: the right ureter was ligated in three cases and suffered a crushing injury in one.

Symptoms and Diagnosis

The most common symptom of ureteral injury, not recognized at the time of surgery, is abnormal urinary leakage. Of 16 cases in which it was present flank pain, fever, or increasing azotemia, indicate possible ureteral injury, and more detailed diagnostic studies should be made. Intravenous pyelography will show whether the kidneys are functioning and whether ureteral and pelvic dilatation is present on one or both sides. It may even demonstrate an abnormal course of one of the ureters. Any abnormal pyelographic finding suggests ureteral injury on the side of the abnormality.

Instillation of indigo carmine into the bladder will demonstrate whether a vesicovaginal or vesicoperineal fistula is present. In either case, the dye is seen coming through the abnormal tract. If there is urinary drainage from the vagina or perineum, but none of the instilled dye comes through, a ureteral fistula may be tentatively diagnosed.

Cytoscopy in the case of a vesical fistula will demonstrate an actual opening in the bladder or may demonstrate necrosis or marked edema in the suspected site. When a ureteral injury or fistula is present, the bladder may appear normal or show only the usual postoperative edema of a mild degree. In the case of a ureteral fistula due to transection or necrosis the ureteral catheter usually meets

TABLE 1.—*Management and Results of Ureteral Injuries Recognized at Time of Surgery*

Primary Disease and Operation	Injury		Corrective Operation	Result
	Side and Site	Type		
Carcinoma of cervix; Wertheim's	Left lower ⅓	Cut	End-to-end anastomosis with intubation	Good
Diverticulitis of sigmoid; abdominoperineal resection	Left lower ⅓	Cut	End-to-end anastomosis with intubation	Good
Carcinoma of sigmoid; anterior resection	Left middle ⅓	Cut	End-to-end anastomosis with intubation	Good
Fibroid uterus; hysterectomy	Right lower ⅓	Ligation and crushing	End-to-end anastomosis with intubation	Good
Carcinoma of rectum; abdominoperineal resection	Left lower ⅓	Cut	End-to-end anastomosis with intubation (silk)	Poor
Carcinoma of cervix; Wertheim's	Right lower ⅓	Cut	End-to-end anastomosis with intubation, with T tube	Poor
Carcinoma of cervix; Wertheim's	Right lower ⅓	Cut	End-to-end anastomosis with intubation, with T tube	Poor

there were 11 ureterovaginal fistulas, 3 ureteroperineal fistulas, and 2 ureterocutaneous fistulas (draining through the abdominal wound). Other symptoms noted in these unrecognized cases were pain in five cases, fever in three, and azotemia in one. Anuria is the predominant symptom if both ureters have been ligated. This situation, however, was not present in any of the cases being reported.

Injury to a ureter at the time of surgery is often diagnosed by direct observation; otherwise, diagnosis must await the onset of symptoms. When there is no urinary output after pelvic surgery, bilateral ureteral ligation should be suspected. This condition must be differentiated from acute renal shutdown due to shock, hemorrhage, or transfusion reaction. When bilateral obstruction is suspected cystoscopy, with passage of ureteral catheters, should be done immediately. If the catheters in the ureters meet obstruction on both sides, a diagnosis of bilateral ureteral injury must be made. If there is no ureteral obstruction, acute renal shutdown is the more likely diagnosis.

Postoperative symptoms of abnormal vaginal, perineal, or abdominal wall leakage, as well as obstruction at the point of injury. Occasionally, the catheter finds its way into the fistulous tract and presents itself through the abnormal opening in the vagina, perineum, or abdominal wall. Radiopaque medium injected through the catheter in the obstructed ureter may find its way into the fistulous tract to be demonstrated roentgenographically.

An incomplete injury or loose ligation of the ureter may allow the catheter to go through the obstructed ureter to the kidney pelvis. Retrograde pyeloureterograms may then demonstrate the point of partial obstruction. If at all possible, retrograde studies of both kidneys should be done to rule out the presence of bilateral injury. Diagnosis of ureteral injury and its exact location thus requires the use of the entire urologic and radiologic armamentarium.

Management

The ureteral injuries in this series can be placed into two categories: those recognized at the time of surgery and repaired immediately (shown in table 1) and those unrecognized and repaired from two weeks to two years later (shown in table 2). Management of most of these accidents was super-

vised by the urologic service. However, a few cases recognized at the time of surgery were managed without urologic consultation.

Seven injuries were recognized and treated immediately. Five were managed by end-to-end anastomosis and intubation, with use of a no. 6 ureteral catheter. The technique used in four cases was as follows: The cut ends of the ureter were trimmed obliquely to prevent a circular constricting scar and then approximated without tension at the anastomosis. With interrupted 0000 chromic catgut on an atraumatic needle, the sutures were limited to the adventitial and muscle layers, an effort being made to avoid the epithelium. In all four cases the site of anastomosis was drained, and the splinting catheter was removed on the seventh postoperative day. All four patients had a successful outcome. Figure 1 illustrates the results in one of these cases. The fifth patient was treated with a similar technique, except that silk instead of chromic catgut was used and the site of anastomosis was not drained. Postoperatively this patient developed a persistent ureteroperineal fistula from the site of anastomosis and ultimately required nephrectomy.

The remaining two patients whose cases were recognized and treated immediately were managed by an end-to-end anastomosis over a T tube, with the long arm brought through the anastomosis and the abdominal wall. Both patients developed persistent ureterocutaneous fistulas and later required nephrectomy.

Sixteen ureteral accidents were not immediately recognized. Of these 12 were surgical accidents and 4 developed after radiation. These cases were managed by different techniques determined by the type, site, and extent of the injury and the status of kidney function. In each case, at the time of exploration and ureteral repair, a biopsy specimen was taken from the site of injury to determine the presence or absence of malignancy.

Ureteroneocystostomy was used as the only reparative treatment in nine cases. This was possible because the injuries were low in the ureter and close to the bladder. Preliminary nephrostomy was done in one of these patients to help control severe infection and to improve kidney function prior to ureteral repair.

Ureteroneocystostomy was done by simply freeing the affected ureter from the surrounding tissues for several centimeters above the site of injury (fig. 2). The ureter was then divided just above the injury (fig. 2*A*). The cut end of the ureter was trimmed, split, and brought through a stab wound (fig. 2*B*) in the bladder wall as close as possible to the trigone (fig. 2*C*). The split edges of ureter were fixed to the bladder wall by fine chromic catgut mattress sutures (fig. 2*D*). The ureter was also fixed to the outer bladder wall with several anchoring sutures through the adventitial and muscle layers (fig. 2*E*). A no. 6 or no. 7 catheter was then passed up the ureter to the kidney pelvis, brought through a midline stab wound, and anchored to a suprapubic drainage tube (fig. 2*F*). This splinting catheter was removed 7 to 10 days later. Of these nine cases results were good in eight and one was a failure, requiring later nephrectomy. The remaining seven patients with unrecognized cases were managed by seven different techniques, as listed in table 2.

TABLE 2.—*Management and Results of Ureteral Injuries Unrecognized at Time of Surgery*

Primary Disease and Therapeutic Procedure	Injury		Interval Before Operation	Corrective Operation	Result
	Side and Site	Type			
Carcinoma of cervix; radiation and Wertheim's	Left lower ⅓	Not known	10 wk.	Ureteroneocystostomy	Good
Carcinoma of cervix; Wertheim's	Left lower ⅓	Not known	3 mo.	Ureteroneocystostomy	Good
Carcinoma of rectum; abdominoperineal resection	Right lower ⅓	Not known	3 mo.	Ureteroneocystostomy	Good
Carcinoma of cervix; radiation	Left lower ⅓	Fibrosis	3 mo.	Ureteroneocystostomy	Good
Carcinoma of cervix; Wertheim's	Left lower ⅓	Not known	2½ mo.	Ureteroneocystostomy	Good
Carcinoma of cervix; Wertheim's	Left lower ⅓	Not known	1 yr.	Ureteroneocystostomy	Good
Carcinoma of rectum; abdominoperineal resection	Right lower ⅓	Cut	2½ wk.	Ureteroneocystostomy	Good
Carcinoma of cervix; radium therapy	Right lower ⅓	Fibrosis	2 wk.	Nephrostomy followed by ureteroneocystostomy	Good
Fibroid uterus; hysterectomy	Left lower ⅓	Crushing	2 mo.	1. Ureteroneocystostomy 2. Ileal substitute for lower ⅔ of ureter	Poor Good
Fibroid uterus; hysterectomy	Right lower ⅓	Not known	4½ mo.	Ureteroneocystostomy and nephrectomy	Poor
Ovarian granulosa cell tumor; right oophorectomy and excision of cervix	Left lower ⅓	Ligation	15 days	Deligation, end-to-end anastomosis, and intubation	Good
Carcinoma of cervix; radiation therapy	Right lower ⅓	Fibrosis	2 yr.	Ureterolysis	Good
Cervicitis and ovarian cyst; removal of cervical stump and salpingo-oophorectomy	Right middle ⅓	Ligation	3½ wk.	Deligation and ureterotomy with T tube	Good
Carcinoma of cervix; Wertheim's	Right, site not known	Not known	6 mo.	Nephrectomy	Poor
Epidermoid carcinoma of vagina; radiation therapy and vaginectomy	Left middle ⅓	Not known	7 mo.	Nephrostomy followed by ureterolysis and intubation	Poor
Carcinoma of cervix; Wertheim's	Left lower ⅓	Not known	8 wk.	Cutaneous ureterostomy followed by nephrectomy	Poor

Results

The results obtained in this series of 22 patients with 23 ureteral injuries are summarized in tables 1 and 2. There were 15 good and 8 poor results. No operative mortality was associated with the ureteral repairs. Whenever a case ended in a nonfunctioning kidney or nephrectomy, the result was classified as poor. The results were considered good only if, after a sufficient follow-up period, the renal function of the involved side was preserved and the patient remained asymptomatic.

Seven ureteral injuries were recognized and treated immediately. Results were good in four cases. Unsatisfactory results occurred in three cases in which some of the basic principles of urologic surgery were not observed; these errors included the use of nonabsorbable suture material, T-tube drainage through the anastomosis, and failure to drain the site of repair.

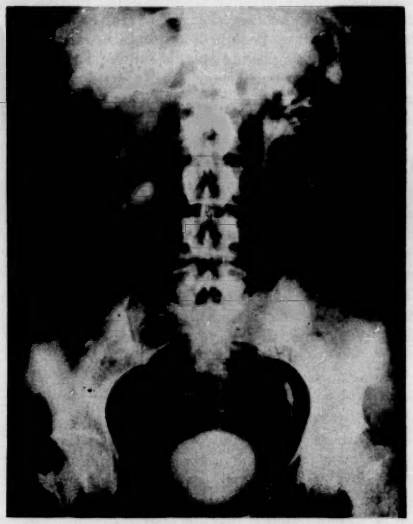

Fig. 1—Postoperative excretory pyelogram of patient after repair of left ureteral injury by end-to-end anastomosis and intubation. Note normal appearance of left collecting system and ureter.

The unrecognized cases in this series were repaired after intervals of two weeks to two years, the average interval being six months. Results were good in 12 cases and unsatisfactory, resulting in a nonfunctioning kidney or necessitating a nephrectomy, in 4. With one exception, the good results were obtained in cases repaired after an average interval of three months and the bad results after an average interval of five months. The exception occurred in a patient with radiation damage, with vaginal urinary leakage for two years. A satisfactory repair was obtained.

Among the 16 unrecognized cases the lower third of the ureter was involved in 13 cases, the middle third in 2, and in one case the site was unknown. Ureteroneocystostomy was carried out in 10 of these patients and good results were obtained in 8. Of the two failures the kidney of one patient was saved by an ileal loop substitute of approximately two-thirds of the ureter during a second reparative operation, and a good result was obtained. The other ureteroneocystostomy which failed, so that the patient ultimately required nephrectomy to stop the urinary leakage, was classified as a failure. The three remaining good results occurred in injuries of the middle part of the ureter in one case and the lower part in two cases. Deligation and an end-to-end anastomosis with intubation was successful in one case. Ureterolysis without intubation was successful in another. The third case was managed by deligation and intubation with a T tube. The long arm of the T tube was brought out through a ureterostomy above the site of injury, and a good result was obtained.

Results were poor in four cases. One involved a ureteroneocystostomy and has been discussed above. A second patient was seen six months after surgery, when urologic study revealed a nonfunctioning, infected, hydronephrotic kidney. No attempt was made to repair the injury and nephrectomy was performed to stop the urinary leakage. In a third patient an emergency nephrostomy was required to combat infection; later, ureterolysis and intubation failed to stop the leakage and a nephrectomy was required. The fourth patient had a cutaneous ureterostomy after exploration revealed a damaged

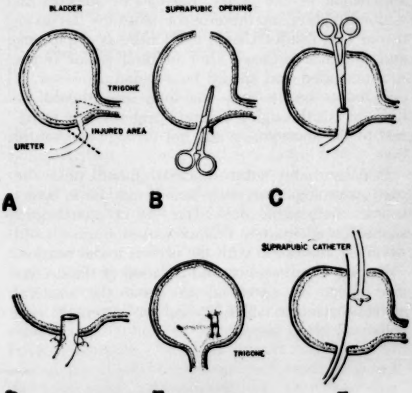

Fig. 2—Technique for ureteroneocystostomy: *A*, ureter is severed proximally to injured area; *B*, with blunt instrument, stab wound is made through bladder wall as close to ureteral orifice as possible; *C*, ureter is pulled into bladder through stab wound; *D*, fine chromic catgut sutures anchor adventitia of ureter to serosa of bladder; *E*, "fish-mouthed" ureter is anchored to bladder epithelium with fine chromic catgut sutures; *F*, ureteral catheter splinted.

segment of ureter approximately 6 cm. from the bladder and too short for end-to-end anastomosis. The surgeon chose cutaneous ureterostomy and later nephrectomy rather than use of an ileal loop or bladder flap to bridge the defect.

Comment

Although ureteral injuries will continue to occur, even with the most experienced surgeons, prophylactic measures can appreciably decrease their incidence.

Preoperative Phase.—Preoperative evaluation of the genitourinary tract by means of excretory and/or retrograde pyelography will reveal such aberrations as congenital anomalies, ureters deviated from their normal course by large tumors or inflammatory masses, and primary incidental urologic diseases. Any one of these factors will render the ureter more susceptible to surgical trauma.

In this institute, indwelling ureteral catheters have been inserted preoperatively only at the request of the various surgical services. Whenever this preoperative measure was employed, no ureteral injury occurred. We believe that the preoperative insertion of indwelling catheters is advisable in all pelvic surgical procedures.

Operative Phase.—The failure to recognize a ureteral injury during surgery eliminates the most favorable time for repair. The longer the time interval between obstruction and repair the less chance the kidney has for recovery.

The technique of repair depends on the site, type, and extent of the injury. End-to-end anastomosis with intubation and ureteroneocystostomy has given us our best results. Use of the T tube as a splinting and drainage catheter after ureteral repair is not recommended and should be avoided; however, if one insists on its use, the long arm should be brought out through a separate ureterostomy proximal to the anastomosis and not through the suture line.

Nonabsorbable suture material should never be used in urologic surgery where it may be in direct contact with urine flow. The site of anastomosis should be adequately drained. Anastomosis should never be attempted with the ureters under tension.

During the dissection and isolation of the ureters care must be exercised to leave the ureteral adventitia intact, since it has an extremely rich collateral blood supply.

Postoperative Phase.—With a preoperative base line of the genitourinary tract available, the postoperative evaluation of these patients enables us to recognize asymptomatic ureteral injuries. Many authors agree that entablishing adequate drainage within two weeks may result in recovery of the completely obstructed kidney. However, when a urinary fiistula occurs, some form of drainage is established which maintains partial renal function and provides more time for repair. Nevertheless, the physician may be lulled into a false sense of security when the fistula spontaneously ceases to drain, for in many such instances this represents the end-result of a ureteral injury, namely, a nonfunctioning kidney.

Conclusions

Because of the anatomic arrangement of the lower part of the ureter there is always danger of injury to it in extensive surgery or irradiation of the pelvis. Preoperative intravenous pyelograms and preoperative insertion of ureteral catheters are the most useful aids in preventing ureteral injuries. The use of these procedures indicates that the operator is alerted to possible ureteral injuries. Early recognition and early repair give the best result.

In the immediately recognized ureteral injuries end-to-end anastomosis with intubation is the preferred treatment. Ureteroneocystostomy gives the best results in the delayed repair of fistulas involving the lower part of the ureter. Adequate drainage and control of infection are essential. Postoperative observation is necessary, since ureteral stricture or loss of kidney function may develop.

40 W. North St. (2) (Dr. Staubitz).

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ACCIDENT PREVENTION IN CHILDHOOD.—Fatal accidents now take a toll each year of about 4,700 children past their infancy but not yet of school age. These deaths account for more than one fourth of the total at ages 1-4. At this early stage of life, accidents cause about twice as many deaths as pneumonia and nearly 3 times the number from cancer in all its forms. This is far from a satisfactory situation even though it represents a substantial improvement over that of only a few years earlier. . . . The primary responsibility for the control of mishaps among pre-school children rests upon their parents. They must provide good supervision, remove hazards, teach simple safety measures, and set good examples at all times. However, physicians, especially pediatricians, are making major contributions in advising parents on the principles of accident prevention and by promoting community programs for child safety.—The Peak in Family Responsibilities, *Statistical Bulletin*, Metropolitan Life Insurance Company, August, 1959.

ACUTE LARYNGEAL OBSTRUCTION IN CHILDREN

Francis W. Davison, M.D., Danville, Pa.

When children develop acute laryngeal obstruction it is important to know promptly whether bronchoscopy and tracheotomy are called for. During a 14-year period 140 cases of acute laryngotracheobronchitis have been treated. Tracheotomy was found necessary in 28 cases. During 1958 steroid therapy was used in 13 cases of acute subglottic laryngitis and, in every case this obviated the need for tracheotomy. A case history illustrates the rapid improvement induced by hydrocortisone given by intravenous drip in infectious subglottic laryngitis in an atopic child. The history of a second case of subglottic laryngitis illustrates the extreme degree of crusting that can occur and the promptness of relief when crusts are removed by bronchoscopy and respiration is eased by tracheotomy. In the experience of the author prompt differential diagnosis, followed by modern methods of treatment, has been lifesaving in nearly every case of acute laryngeal obstruction in children.

Croup is the diagnosis most frequently made when a physician sees a child with acute laryngeal obstruction. This diagnosis is inadequate because there are at least six different causes of acute obstruction. Fatalities can be prevented if the correct diagnosis is made early and if proper therapy for the cause of the obstruction is promptly initiated. Terminology is important. I prefer a classification which indicates the anatomic site of the obstruction as well as the cause of the obstruction, because it fixes attention on the factors that must be promptly corrected if unnecessary tragic fatalities are to be prevented.

Some years ago I advocated [1] the following classification of acute laryngeal obstruction in children: (1) acute obstructive supraglottic laryngitis (acute epiglottitis, edematous septic laryngitis, influenzal laryngitis, and edema of the glottis); (2) supraglottic allergic edema (angioneurotic edema); (3) laryngeal diphtheria (membranous croup, true croup, and diphtheritic croup); (4) subglottic allergic edema (spasmodic croup, spasmodic laryngitis, false croup, catarrhal spasm of the larynx, and laryngismus stridulus); (5) acute laryngotracheobronchitis (subglottic laryngitis, and nondiphtheritic croup) and virus croup [2]; and (6) foreign body in the larynx or upper trachea.

I was glad to see this classification copied in one of the pediatric textbooks,[3] because pediatricians, who often see these children first, must recognize the different types of obstruction and must know promptly when to call an otolaryngologist who has the ability to introduce a bronchoscope and perform a tracheotomy.

Each of these forms of acute laryngeal obstruction causes the classic symptoms of stridor, retraction of the soft tissues above the clavicles and in the epigastrium during inspiration, and elevated pulse and respiratory rates, but the urgency of treatment and type of treatment depend on the type of disease present.

Acute Obstructive Supraglottic Laryngitis

Acute obstructive supraglottic laryngitis (acute epiglottitis) [4] is a term applied to inflammation involving chiefly the epiglottis and aryepiglottic folds. It is a clinical entity and should be distinguished from all other types of acute laryngeal obstruction because it develops with great rapidity. Only four or six hours may elapse from the first symptom until the time tracheotomy is urgently needed. Failure to recognize this fact may lead to a fatality, as is evidenced by the following case report.

Case 1.—This child, a male, aged 2½ years, was in good health until eight hours before admission, when he had an emesis and was noted to have a temperature of 103 F (39.4 C). Two and one-half hours prior to his admission on the pediatric service, his respirations became noisy and rapid. The pulse rate on admission was 140 and the respiratory rate 56 per minute. While a lumbar puncture was being attempted, the child ceased breathing. An emergency tracheotomy was performed, but respirations were not reestablished. One hour had elapsed from the time of admission until the time of death. Much work had been done, as evidenced by the large number of laboratory reports in the chart, but the child died because the attending physician did not know that a child with epiglottitis can breathe reasonably well sitting up and yet breathing can become totally obstructed by the swollen supraglottic structures when the child is placed in the horizontal position, which was used to permit performance of the lumbar puncture. For those who place great faith in the importance and veracity of cultures, I cite the following facts. This

From the Department of Otolaryngology and Broncho-Esophagology, the George F. Geisinger Memorial Hospital and Foss Clinic.

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child's nose culture showed Diplococcus pneumoniae, the throat culture showed a beta hemolytic streptococcus, and the blood culture showed Hemophilus influenzae.

Comment.—The clinical picture is usually recognizable without direct laryngoscopy, and direct laryngoscopy should be done only by someone who has at hand a 3.5-mm. or 4-mm. bronchoscope and knows how to introduce it rapidly and safely. The fiery red, tremendously swollen epiglottis can be seen if the child is examined while being supported and restrained in the sitting position if the examiner uses a headlight and a small, child-size metal tongue blade. If it is done skillfully and quickly there will be only momentary increase in dyspnea. These children should not be restrained in the supine position.

With this type of obstruction there is stridor on inspiration and a coarse, fluttering sound during expiration, due to vibration of the swollen aryepiglottic folds. A croupy cough is never present because a croupy cough is due only to subglottic swelling. I have never seen epiglottitis and subglottic edema in the same patient. Respirations are apt to be relatively slow in proportion to the pulse rate, because the patient has learned that rapid or forceful inspiration sucks the edematous aryepiglottic folds into the larynx and thus increases the obstruction. Pale cyanosis is often present. The shock-like picture described by some authors is, in my opinion, due to hypoxia. I say this because it clears up immediately after introduction of a bronchoscope and performance of tracheotomy. The technique of tracheotomy is well described by Galloway.[5] Oxygen is no substitute for tracheotomy but may be used as a temporary measure. These children have inspiratory stridor as well as the coarse fluttering sound during expiration, but there is seldom true hoarseness. As Miller [4] says, these children insist on sitting up and extend the head forward in order to increase the greatly narrowed supraglottic airway. Older children will complain of pain in the throat. Swallowing is very difficult, so saliva drools from the mouth. Use of a humidified tent is not necessary for patients having supraglottic laryngitis, unless a tracheotomy has been done.

This type of infection is usually, but not always, due to H. influenzae, type B. Therefore, after tracheotomy, the most important part of the treatment is use of streptomycin given intramuscularly, 20 mg. per pound of body weight per day in divided doses every six hours, and penicillin given intramuscularly. I prefer fortified procaine penicillin G, 1 million units given intramuscularly every six hours. The antibiotics selected should be given by injection to insure prompt absorption. There was only one death in my series of 20 cases of epiglottitis, and that was due to delayed tracheotomy. Ten patients required tracheotomy.

Supraglottic Allergic Edema

Allergic edema involving the supraglottic structures (angioneurotic edema) can develop with great rapidity and present exactly the same clinical picture as that caused by acute supraglottic laryngitis, but direct laryngoscopy shows a pale watery edema of the epiglottis and the aryepiglottic folds in contrast to the fiery red edema seen when the obstruction is due to acute supraglottic laryngitis. Allergic edema will usually respond quickly to parenteral administration of epinephrine, but in one case it was necessary to insert a bronchoscope and leave it in position for a period of 15 minutes until the edema had subsided sufficiently to permit unembarrassed respiration.

In one case the acute supraglottic allergic edema in a 6-year-old boy was the result of antitetanic serum given 10 days previously. The edema subsided quickly in response to 0.2 cc. of 1:1,000 aqueous solution of epinephrine given subcutaneously.

Laryngeal Diphtheria

Laryngeal diphtheria sometimes occurs when there is no membrane visible on the pharynx or tonsils so that accurate diagnosis must depend on direct laryngoscopy confirmed by smears and cultures. However, certain points in the history and physical examination should lead the examiner to suspect its presence. Usually diphtheritic laryngitis is slow in development, with a lapse of two or three days from the onset of hoarseness until dyspnea is sufficiently marked to require tracheotomy. Usually the temperature is not high and may be no more than 100 or 101 F (37.8 or 38.3 C). The cry is hoarse because normal vibration of the cords is hampered by the presence of membrane.

A specimen for smears and cultures can be most conveniently obtained by using an aspirating collector through a direct laryngoscope. If there is a membranous type of exudate or if direct smears show positive results for the presence of diphtheria organisms, it is advisable to give antitoxin without waiting for the culture report. Further details of the management of diphtheritic cases may be found in any of the standard pediatric textbooks.

Subglottic Allergic Edema

Characteristically, children with subglottic allergic edema (spasmodic croup, laryngeal stridor, spasmodic laryngitis, or false croup) awaken at night with dyspnea, croupy cough, and inspiratory stridor. They usually have been quite well the preceding day or may possibly have had a little rhinitis but no fever. By morning the symptoms have cleared up, only to recur the next night and possibly for several succeeding nights. For generations this clinical picture has been referred to as spasmodic croup, the inference being that the obstruction is due to adductor spasm of the vocal cords. This concept is erroneous for the following reason.

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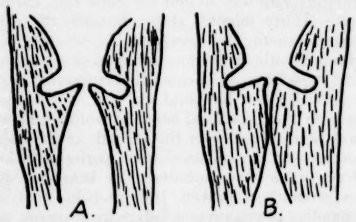
The sound of the croupy cough is identical with that produced by the subglottic swelling seen by direct laryngoscopy in cases of acute laryngotracheitis.

The diagrams in the figure show coronal sections of a normal larynx and the location of the subglottic swelling which produces a croupy cough. This swelling may be due to a transient allergic edema or to the indurated submucosal inflammation present in cases of infectious subglottic laryngitis.

In a few cases of so-called spasmodic croup that I have observed in hospital practice, direct laryngoscopy showed pale watery edema of the subglottic tissues, and the obstructive symptoms cleared up within 15 minutes after subcutaneous administration of 0.2 cc. of aqueous solution of epinephrine. The rapid onset and later improvement in one to four hours in these patients having subglottic allergic edema is quite comparable to the transitory nature of hives in the skin. Croup has been referred



A, coronal section of a normal larynx. B, coronal section showing subglottic swelling, which is only cause of croupy cough; it may be due to allergic edema or to indurated submucosal swelling of acute laryngotracheitis.

to as a manifestation of allergy by Vaughan,[6] Rowe,[7] Cohen,[8] Spain,[9] Urbach,[10] and other physicians who are experienced in dealing with allergic persons.

I have suggested the term subglottic allergic edema for this malady because it is descriptive of both the anatomic location and the etiology. It is distinguished from other forms of obstructive laryngitis by its sudden onset and by the complete or almost complete remission of symptoms during the daytime.

All physicians to whom I have suggested the use of epinephrine for treatment of nocturnal spasmodic croup have reported that it was effective and have said in addition that use of diphenhydramine (Benadryl) hydrochloride saved them many night calls for children who were subject to croup.

Acute Laryngotracheobronchitis

Acute laryngotracheobronchitis (subglottic laryngitis) most often begins as primary subglottic laryngitis. The children have a dry, croupy cough and inspiratory stridor produced by subglottic swelling. In almost all cases the sound of the cry is clear, indicating that the edges of the vocal cords are normal and free from membrane. The temperature varies from 100 to 105 F (37.8 to 40.5 C). The dyspnea becomes progressively worse over a period of one to seven days before it is severe enough to require admission of the child to a hospital.

Many of the patients have had previous head colds. Head colds cause nasal obstruction and mouth breathing so that the extremely dry indoor air in winter impinges directly on the larynx without having previously been moistened by passage through the nose.

The pathological changes observed by means of direct laryngoscopy and bronchoscopy are redness and swelling of the lateral walls of the trachea just below the vocal cords so that the subglottic space is reduced to an anteroposterior slit 1 to 2 mm. wide. Often the subglottic tissues are coated with a layer of dry, rough, gray adherent exudate which extends downward 0.5 in. below the level of the cords and increases the obstruction. Usually this exudate does not have the appearance of diphtheritic membrane. The swelling of the subglottic tissues is firm and indurated as is demonstrated by the fact that it requires considerable pressure to introduce even a 3.5-mm. bronchoscope. This subglottic swelling is not due to simple watery edema but to infiltration of the submucous tissues of the conus elasticus with inflammatory cells, as postmortem examinations have shown. Holinger [11] has called our attention to the fact that the subglottic tissues are surrounded by a firm cartilaginous ring, so that inflammatory swelling can take place only at the expense of the airway.

Our cultures and those of many other observers [12] indicate that any of the pathogenic gram-positive cocci can be the bacterial agent responsible for this disease. Moreover, smears made from the intratracheal exudate aspirated through the bronchoscope introduced just prior to tracheotomy showed gram-positive cocci mixed with neutrophils, so it seems unnecessary to postulate a virus infection as the cause of the disease. In addition, most patients have shown such prompt response to treatment with penicillin that it seems evident that the infection is due to penicillin-sensitive organisms. The viral origin of acute subglottic laryngitis has been stressed by Rabe.[2] It is, of course, possible that a virus initiates the infection. This is an academic concept of no practical importance because it does nothing to help us prevent or cure the infection.

Treatment

The most urgent part of treatment is relief of airway obstruction. The patients are placed immediately in a humidified oxygen tent. The relative humidity should be at least 90%, with the temperature maintained between 70 and 75 F.[13] The high humidity helps to maintain the fluidity of the tracheobronchial secretion and tends to soften

the crusts adherent to the subglottic mucosa so that they can be coughed out. We frequently see rapid improvement in the airway within two hours after a child has been placed in a humidified tent.[14] The nurse is instructed to count and record the pulse and respiratory rates every 15 minutes. I regard a pulse rate of over 140 or a respiratory rate of over 40 per minute as a danger sign. If the pulse and respiratory rates continue to increase or do not decrease during the first three hours after the child is placed in the humidified tent, it is probable that tracheotomy will be required. If there is obvious urgent dyspnea accompanied by the pale gray type of cyanosis at the time of admission, a small bronchoscope is introduced and tracheotomy performed immediately before the child is placed in the tent.

The following case report illustrates the extreme degree of crusting that can occur and shows why introduction of a flexible endotracheal tube is not as satisfactory as introduction of a bronchoscope just prior to tracheotomy.

Case 2.—An 8-year-old boy was admitted in an almost moribund state. He was pale and irrational and had rapid shallow noisy respiration. There was marked indrawing of the soft tissues in the suprasternal notch and in the epigastrium with each inspiratory effort. Immediate direct laryngoscopy showed marked redness and swelling of the lateral walls just below the vocal cords. Hard, dry adherent crusts almost filled the remaining airway. A 5-mm. bronchoscope was introduced, and the crusts were removed with aspirator and forceps. An orderly tracheotomy was then performed. After five minutes, the boy sat up and drank a cup of water. Cultures from the endotracheal exudate showed a beta hemolytic streptococcus. The temperature, which was 103 F (39 C) on admission of the patient, returned to normal in less than two days. Additional treatments were used with a humidified tent; fortified procaine penicillin G, 1 million units by intramuscular injection every four hours; and streptomycin, 0.25 Gm. by intramuscular injection every eight hours. The tracheal cannula was removed on the sixth day, and the patient went home on the eighth day.

Comment.—Some physicians fear tracheotomy because they have seen fatalities follow it; hence they tend to procrastinate and thereby seriously jeopardize the life of the patient. In my experience there are only two causes of death after tracheotomy. These can be entirely avoided if the correct diagnosis is made and proper treatment promptly instituted. The two causes are pneumothorax and crusting in the trachea and bronchi. Both conditions are correctible if diagnosis is made early.

Crusting in the trachea is too often the result of overzealous use of the aspirating catheter introduced through the tracheal cannula. To prevent destruction of the ciliated epithelium of the trachea by the aspirating catheter, I put a collar of adhesive tape around the catheter in such a position that the tip cannot be introduced deeper than 0.25 in. below the lower end of the tracheal cannula. Crusts that occasionally form despite use of a humidified tent can be loosened by dropping 5 to 15 cc. of Ringer's solution in the cannula and then placing the child in a head-low position. Further information is given by Galloway.[15]

Pneumothorax sometimes develops spontaneously before tracheotomy and sometimes is the result of injury to the dome of the pleura during tracheotomy. In either event, if the pneumothorax is promptly recognized and air is aspirated from the pleural space there will be no fatality. The following case report illustrates this type of complication.

Case 3.—A 3-year-old boy was admitted on the pediatric service with a chief complaint of croup. Symptoms had been present for only 24 hours prior to admission. Six hours prior to admission the difficulty in breathing became severe. On admission the temperature was 99.6 F (37.5 C); the respiratory rate was 40 and the pulse rate 120 per minute. Thirty minutes after admission the child became cyanotic. An emergency tracheotomy was performed without previous insertion of a bronchoscope. A no. 2 tracheal cannula was inserted without difficulty, but the child still had a pale ashen gray type of cyanosis and labored breathing. Breath sounds were absent over the left side of the chest. Thoracentesis was immediately performed, and 200 cc. of air was aspirated. The breathing and color promptly improved. It is probable that the pneumothorax was present before tracheotomy and was the cause of the sudden attack of cyanosis which prompted the tracheotomy. His convalescence was uneventful.

Comment.—If one is uncertain about the presence of pneumothorax or mediastinal emphysema, one should request prompt roentgenographic examination. Orton [16] always made it a rule to request roentgenographic examination immediately after every tracheotomy.

One of the most important recent advances in treatment has been the use of steroids. During 1958 we had 13 cases of acute subglottic laryngitis in our hospital. Medical treatment resulted in the avoiding of tracheotomy in all 13 cases. Two of these patients were given hydrocortisone intravenously and three were given prednisone, 5 mg. by mouth every eight hours. In addition, one patient with supraglottic laryngitis was given hydrocortisone intravenously, in addition to penicillin and streptomycin intramuscularly. All six of these patients had a spectacular improvement in the airway and marked reduction in the temperature within 12 to 24 hours. The following case report illustrates the value of hydrocortisone given intravenously.

Case 4.—A 6-year-old boy had fever for five days and cough and marked difficulty in breathing for 12 hours prior to admission. His temperature was

104 F (40 C); his pulse was 160 and respiration rate 60 per minute. There was marked retraction of the soft tissues above the clavicles and in the epigastrium during inspiration. Mirror examination showed marked redness and swelling of the lateral walls of the conus elasticus, so the airway was a slit only 2 mm. wide. The obvious diagnosis was severe acute subglottic laryngitis. The treatment used was therapy with hydrocortisone, 100 mg. in 1,000 cc. of 5% dextrose solution, by intravenous drip over an eight-hour period; a humidified tent; and penicillin and streptomycin given intramuscularly. In 12 hours the temperature was 98 F (36.7 C), the pulse 110, and the respiratory rate 24 per minute. The culture showed a beta hemolytic streptococcus. This child was known to have seasonal allergic rhinitis. I have never before seen such rapid improvement in a child with severe acute subglottic laryngitis.

Data on 140 Patients with Acute Laryngotracheobronchitis During Fourteen-Year Period

Year	Cases, No.	Tracheotomies, No.
1942	8	2
1943	8	5
1944	14	4
1945	13	4
1946	8	0
1947	6	0
1948*	9	2
1949	8	1
1950	17	2
1951	10	1
1952	1	0
1953	3	1
1954	3	0
1955	5	3
1956	4	1
1957	10	2
1958	13	0
	140	28

* One death occurred in 1948; no deaths in other years.

Comment.—Infections in allergic persons are usually characterized by rapid onset, violent course, and slow regression. The use of steroids quickly reduces the submucosal edema in both supraglottic and subglottic laryngitis.

The low mortality in this series of patients (see table) having acute laryngotracheobronchitis (subglottic laryngitis) is attributed to careful personal attention to each patient, large intramuscularly given doses of penicillin (3 to 5 million units daily), safe intramuscularly given doses of streptomycin (20 mg. per pound of body weight per day), cool (72 F) moist air, early tracheotomy, avoidance of catheter trauma to the mucous membrane of the trachea, and postural irrigation [15] with saline solution.

Foreign Bodies in Larynx or Upper Part of Trachea

In these cases the severity of the obstruction will depend on the size of the object and the traumatic or infectious edema which develops subsequently. If roentgenographic examination does not give a clear-cut answer to the presence or absence of foreign body, direct laryngoscopy and tracheoscopy should be done promptly to remove the object or to make certain that one is not dealing with a purely infectious type of obstruction.

The presence of a foreign body in the trachea should always be considered when one sees a dyspneic child. A wheeze heard at the open mouth is usually present in such cases.

Summary and Conclusions

Prompt differential diagnosis, followed by modern methods of treatment, will prevent death in nearly every case of acute laryngeal obstruction in children. Acute supraglottic laryngitis may require tracheotomy within four hours of the onset of the first symptom. Tracheotomy after introduction of a bronchoscope is the treatment of choice when obstruction is marked.

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PERIPHERAL NEUROPATHY AFTER EXPOSURE TO AN ESTER OF DICHLOROPHENOXYACETIC ACID

Norman P. Goldstein, M.D., Peter H. Jones, M.R.C.S., L.R.C.P.
and
Joe R. Brown, M.D., Rochester, Minn.

Severe sensory and motor symptoms necessitated hospitalization of three patients, a 52-year-old man, a 50-year-old woman, and a 65-year-old man. In each case the disorder began some hours after the use of preparations of dichlorophenoxyacetic acid (2,4-D) to kill weeds; the symptoms progressed through a period of days until pain, paresthesias, and paralysis were severe. Disability was protracted, and recovery was incomplete even after the lapse of years. There was little doubt that the neurological damage was done by the percutaneous absorption of spilled 2,4-D. The electromyographic examination supported the diagnosis of peripheral neuropathy. Since there is no antidote or other specific treatment for 2,4-D poisoning, this herbicide should be used with caution.

Disease of the peripheral nerves has been shown in the past to follow exposure to various heavy metals, organic solvents, and medicaments.[1] These substances are often used in industry and in the practice of medicine. With the synthesis of new compounds for both industrial and clinical use, it is likely that additional compounds will be shown to produce disease of the peripheral nervous system.

In three cases of polyneuritis the history indicated that exposure to the herbicide dichlorophenoxyacetic acid (2,4-D) preceded the development of the neuritis. The time relationship was such that it seemed reasonable that the herbicide caused the neurological disease.

Report of Cases

CASE 1.—A 52-year-old farmer registered at the Mayo Clinic on Oct. 10, 1955, with the chief complaints of weakness, paresthesia, and aching in all four extremities. Five months prior to our examination, he had spilled about 2 fl. oz. (60 cc.) of a 10% solution of an ester of 2,4-D on his forearms. He had failed to wash it off, and that evening he had felt unduly fatigued. A few days later, nausea and vomiting had developed. These symptoms had lasted for 10 days, and during this time the patient had lost 20 lb. (9.1 kg.) in body weight.

About two months later, while again using the same concentration of this herbicide, the patient accidentally had wetted his legs with it. Over the next five days nausea and vomiting had developed and also diarrhea. A week after this second exposure to the herbicide, the patient had noted numbness and aching in the fingers and toes of both right and left extremities. He had been hospitalized. The sensations of numbness and aching gradually had extended proximally from the fingers to involve the hands, and in the lower extremities they had reached the lower part of the thighs. During the next four weeks, the fingers and toes had become more numb, and shooting pains had developed in both feet, the right foot being more painful than the left. The pain had been severe enough to require the use of narcotics. In addition, there had been desquamation of the skin of the palms and soles.

From the Section of Neurology, Mayo Clinic and Mayo Foundation. Dr. Jones is a Fellow in Neurosurgery, Mayo Foundation. The Mayo Foundation is a part of the Graduate School of the University of Minnesota.

Approximately six weeks after the second exposure to 2,4-D, the condition had progressed so far that the patient was unable to walk because of the pain and weakness in both legs. He had lost sensation in both intestine and bladder but was able to urinate and control his bowel movements. An examination of cerebrospinal fluid was said to have shown an increased concentration of protein.

At the time of his admission to the Mayo Clinic, the findings on the patient's general examination were satisfactory. The neurological examination disclosed the presence of a flaccid quadriparesis that was more severe in the lower extremities. There was a sensory deficit of the hands and forearms, with moderate impairment in perception of pain, light touch, and temperature. In the lower extremities there was a similar sensory disturbance from the mid-thigh downward. Joint sensation in the fingers and toes was absent, as was appreciation of vibratory stimulation at the ankles. The muscle stretch reflexes were absent. Testing for the Babinski sign elicited no response on either side.

The hemoglobin concentration, leukocyte count, and erythrocyte count, the results from urinalysis, and the serologic test for syphilis were normal, as was the result from a sulfobromophthalein (Brom-

sulphalein) test of liver function. Examinations of the urine for porphyrins and for arsenic disclosed none; the lead concentration per liter of urine measured 0.03 mg.

This patient returned for reexamination on Sept. 18, 1957, stating that his condition had improved gradually in the two intervening years. By January, 1956, he had progressed sufficiently to be able to walk with the aid of crutches. In the spring of 1956 he had returned to part-time farm work. Approximately one year later he had been doing full-time work on the farm "except for heavy lifting." His complaints in September, 1957, included (1) "numbness" of the feet and fingers, (2) inability to move his toes, and (3) aching of the feet.

The neurological examination revealed marked improvement. The patient had only slight difficulty in walking on his toes and heels, although he was unable to hop on either foot. The muscle stretch reflexes were slightly hypoactive in the upper extremities; the quadriceps reflex was moderately decreased bilaterally, and the ankle reflexes were absent. Muscular strength was normal, except for slight weakness of the muscles of the lower parts of the legs and inability to move the toes. Findings on the sensory examination were normal, except for subjective hypesthesia and hypalgesia of the feet; joint sensation was normal in the feet, but vibratory sensation was moderately diminished at the ankles. An electromyogram showed only minimal denervation in the right gastrocnemius and decreased motor unit activity in the left extensor digitorum longus.

The patient wrote to us on Oct. 30, 1958, informing us that his legs had become stronger, although he still could not move his toes, and that the paresthesia of his feet and fingers had lessened.

Case 2.—A 50-year-old bookkeeper and housewife registered at the Mayo Clinic in October, 1955, with the chief complaints of weakness and numbness of both legs. She had been well until the spring of 1954. Just prior to the onset of her illness she had sprayed dandelions with a solution of an ester of 2,4-D, kneeling on the ground to do so. In the process her hands and legs had become wet with the herbicide. Shortly after this, she had noted swelling and aching of her feet and legs that had persisted for about two and one-half weeks. Rest in bed had given complete relief. The patient had been well from then until May, 1955, when after a similar exposure to the herbicide similar symptoms had occurred. She had continued to work, and the swelling had progressed to involve the knees. Her legs had not changed color, but they had felt warm.

The patient had been hospitalized for one week for observation. On the night of her discharge from the hospital excruciating pains had developed in her legs and a painful swelling in the metacarpal joints of both hands, necessitating rehospitalization that same night. While in the hospital she had been affected considerably by anorexia and had lost 20 lb. (9.1 kg.) in body weight. No fever or jaundice had been noted.

Therapy with cortisone had been started but was discontinued when the patient became agitated and depressed and had frequent crying spells. After three weeks she had returned home but had been unable to walk.

In August, 1955, there had been an episode of diarrhea of unexplained origin. After admission to a hospital for physical therapy, she had noted a rash in the groin that had spread to the thighs. The rash had itched, and a few bullae filled with serous fluid had developed. After the beginning of physiotherapy the numbness of the extremities had lessened gradually, but stiffness of the legs and difficulty in walking had persisted.

At the Mayo Clinic, the findings on the general medical examination were normal. The neurological examination revealed a flaccid paraparesis, with marked weakness of the lower part of the legs. Sensory tests of touch, pain, and temperature disclosed a moderately severe sensory deficit. The sensory loss was more marked in the feet than in the legs. In the upper extremities were a sensory loss corresponding to the ulnar nerve distribution in the left hand, and a weakness of the intrinsic muscles of both hands. The Achilles reflexes were absent, but the other tendon reflexes were not unusual.

The hemoglobin level and the erythrocyte and leukocyte counts were normal. Albuminuria, with albumin content of grade 2, was the only unusual finding in urinalysis. The result of the serologic test for syphilis was negative. The fasting blood sugar level was normal. Findings from tests for lead, arsenic, and porphyrins in the urine were negative.

An electromyographic study showed denervation in several peripheral muscles, with typical fibrillation potentials. The proportion of polyphasic motor unit potentials was above normal. The velocity of conduction was slower than normal in the left ulnar nerve (37 meters per second).

On Nov. 21, 1958, we received information about this patient from her family physician. She had improved, although she still had some pain in the legs. She was able to walk but was clumsy on her feet. The paresthesia also had lessened. She was able to do her own housework, despite the fact that she had fallen and fractured one arm. In general, she was considered to be approximately two-thirds recovered from her worst stage in 1955.

Case 3.—A 65-year-old farmer registered at the Mayo Clinic on Oct. 13, 1955, with the chief complaint that pain in the lower extremities and twitch-

ing of muscles had persisted for five months. Prior to the onset of this complaint, he had spent two days spraying a cornfield with a solution of an ester of 2,4-D. During this time his sleeves and trouser legs had been wetted with the herbicide. On the next day increasing malaise, headache, nausea, and finally vomiting had made him retire early. On the following day vertigo had prevented his standing, and vomiting had been frequent. After four or five days he had felt generally improved, but at this time he had noted paresthesia of the extremities and pain in the legs, as well as twitching of the muscles of the calves and arms. He described the paresthesia and muscle twitching as a "feeling of worms crawling beneath the skin." Gradually the fasciculations had become more pronounced, until all skeletal muscles were involved. No muscular weakness had been noted.

General examination revealed old healed pulmonary tuberculosis, chronic glomerulonephritis, and atrophy of the right testis. The blood pressure was 120 mm. Hg systolic and 80 mm. Hg diastolic. Neurological examination revealed generalized, extensive fasciculations that were fine to coarse. No objective sensory or motor deficit was found. No evidence of disturbance of the autonomic nervous system was noted. Funduscopic examination disclosed minimal changes of hypertensive sclerosis.

The concentration of hemoglobin and the counts of erythrocytes and leukocytes were within normal limits. The sedimentation rate was 41 mm. in one hour (Westergren method), and the blood urea level 40 mg. per 100 ml. In the urine no arsenic and only 0.04 mg. of lead per liter were found. Urinalysis showed persistent albuminuria and occasional casts. On examination of the cerebrospinal fluid, the findings from manometric studies were normal, as was the appearance. The concentration of protein was 65 mg. per 100 ml., one lymphocyte was present, the Wassermann reaction was negative, and the colloidal gold curve was 0000000000.

An electromyogram (made by Dr. E. H. Lambert) showed no evidence of denervation. The velocity of conduction of the left peroneal nerve was slightly slowed (38 meters per second). Motor unit potentials were normal. Fasciculations were of the grouped discharge type and similar to those that can be caused by drugs such as neostigmine.

This patient returned for reexamination on Aug. 24, 1956. He stated that he had constant pain in the upper and lower extremities. He had stopped working in November, 1955, because of the pain. The fasciculations had persisted. Prednisone therapy for three months had not lessened the pain or fasciculations, and he was taking codeine to control the pain. Minimal paresthesia was present in all four extremities.

The findings from neurological examination were essentially unchanged, except for a slight decrease in perception of vibratory stimuli at the ankles. An electromyographic examination indicated no significant change from the status disclosed by the previous examination.

Comment

In all three of the cases reported above, symptoms and signs of a general toxic reaction as well as involvement of the peripheral nervous system developed after exposure to an ester of 2,4-D. So far as we know, there have been no other reports of a toxic reaction to this substance in humans. Hildebrand [2] mentioned that some investigators consumed unreported amounts of 2,4-D and suffered no ill-effect. He also stated that the 2,4-D solution is not irritating to the skin.

Hill and Carlisle,[3] however, in autopsies on animals subjected to chronic poisoning, found renal edema with tubular changes; in some dogs they also found evidence of damage to the liver. Bucher [4] noted the production of temporary myotonia in several species of laboratory animals after a single injection of 2,4-D. He did not find any striking change on histological examination of various organs, but he did note that parenteral administration in dogs caused sneezing, lacrimation, and rubbing of the eyes, as well as a gastrointestinal disturbance with vomiting and anorexia. In mice, besides the myotonia and other reactions found in dogs, there were diarrhea, sluggishness, reluctance to move, rigidity of the tail, and a coarse clonic tremor. Coma and death followed in some animals, while others recovered without residual neurological deficits.

Sollmann [5] has said that a syndrome of myotonia, stiffness of the extremities, ataxia, lethargy, paralysis, and coma may follow the parenteral administration of 2,4-D in experimental animals. Large doses may cause ventricular fibrillation also.

In plants, a concentration of 10 ppm of 2,4-D stimulates growth. When the concentration is increased to between 100 and 1,000 ppm, the excessive stimulation of growth kills the deep root system.[5] It has been postulated that the metabolism of phosphate is interrupted or inhibited.

In our patients the toxic substance entered through the skin and possibly also by way of the respiratory system. The 2,4-D had been diluted, but still, with wetting of the extremities and the clothing, the exposure apparently was greater than usual. The involvement of the peripheral nervous system could be a result of a direct toxic effect, or possibly a sensitivity reaction, such as that seen after the injection of a vaccine or an antitoxin. At present, the mechanism of toxicity that follows exposure of mammals to 2,4-D is not known.

In order to prevent further cases of neuropathy from this herbicide, it seems logical to recommend shorter periods of exposure, frequent washing of the skin, and changing of clothes when they be-

come wet with the solution. No antidote is known, and there seems to be no specific treatment for the neuropathy if it develops.

Summary

Three cases of polyneuritis occurred after heavy exposure to an ester of dichlorophenoxyacetic acid (2,4-D). The mechanism of the toxicity affecting the peripheral nervous system is unknown. There is no antidote and no specific treatment.

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THE PROCTOLOGIST AND THE PRACTICE OF MEDICINE

A. W. Martin Marino, M.D., Brooklyn, N. Y.

There is evidence that proctology was practiced in ancient times and existed even then as a specialty. Nevertheless a proctologist should be a physician first and a specialist second. There are many conditions, such as pruritus ani and hemorrhoids, that should not be treated locally until there has been a general search for causative factors. Conversely there are many conditions that should not be treated systemically until the physical examination has included a proctologic survey for the diagnostic information it may yield. Specialties rise as their need arises and fall for lack of usefulness. Proctology is a much-needed specialty, but physicians must never forget that, whatever their regions of special interest, they are treating human beings and not just diseased parts of people.

While ours is called the "age of specialization," a look back through the centuries reveals that specialization had developed to a marked degree in the earliest times of which there is any record. Imhotep, an Egyptian of the third dynasty (about 3000 B. C.), the earliest known physician, was especially skilled in relieving pain by producing sleep. Herodotus of Halicarnassus, the Greek historian, reporting his travels in Egypt in the fifth century B. C., recorded the following statement (same meaning given by various translations):

> The art of medicine in Egypt is thus exercised: each physician is confined to the study and management of one disease only; there are of course a great number who practice this art; some attend the disorders of the eyes, others to those of the head, some take care of the teeth, others are conversant with all diseases of the bowels; whilst many attend to the cure of maladies which are less conspicuous.

As a general rule, however, practitioners who were especially skilled in a branch of medicine in ancient times were not necessarily "full specialists" as we define specialists today. They were apt to be men who were more proficient in one phase of practice and devoted more time to that phase in the course of their general practices.

Pioneers in Endoscopy

The means to inspect adequately and to explore visually the hollow viscera, such as the urinary bladder, trachea and bronchi, esophagus, and the large intestine, for diagnostic and therapeutic purposes, was made possible by ingenious men of vision with inquiring minds. The urologists were the pioneers in such work. It was Philip Bozini who in 1805 devised the first endoscope, which he called the *lichtleiter*, an illuminating tube with which to see inside the urinary bladder.

It was not until 1895 that the first proctoscope and sigmoidoscope were introduced, and it remained for Howard Atwood Kelly of Johns Hop-

From the Department of Surgery, Division of Proctology, the Brooklyn Hospital, and the Department of Surgery, State University of New York Downstate Medical Center College of Medicine.

Chairman's address, read before the Section on Gastroenterology and Proctology at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 11, 1959.

kins to do so. The proctoscope was 6 in. in length and the sigmoidoscope 8 in. long. Illumination was obtained by means of reflected light with a head mirror. Hermann Strauss of Berlin in 1910 improved Kelly's endoscope by adding an inflating device. Up to that time the distending effect of atmospheric air was depended on to help balloon out the rectum. It was not long before very practical electrically lighted proctoscopes and sigmoidoscopes became available. The lighting has been improved to the degree that instruments 12 in. in length and longer can be introduced through the anus in suitable patients for exploration of the sigmoid and rectum. Modern proctoscopes are 8 to 10 in. long, and sigmoidoscopes are 10 to 12 in. long. There are instruments that can reach higher in selected patients, but these instruments are not practical for ordinary use. In his "Traite' D'Endoscopie," in 1926, Bensaude makes the following statement:

> Rectocolic endoscopy such as we practice today in Europe, is entirely due to the work of American authors, and the outcome of this mode of exploration, inaugurated by Desormeaux, may be compared to that of intubation, which born in France with Bouchut's investigations, was completely forgotten there until the day it came back from America with the instruments perfected by O'Dwyer.

Earliest Records of Proctologic Disorders

Wide prevalence of diseases of the colon, rectum, and anus was recorded in the earliest writings with which we are acquainted. In the Code of Hammurabi (about 2200 B. C.) is found the following statement: "If a doctor . . . has cured the diseased bowel, the patient shall give five shekels of silver to the doctor." Eber's papyrus from Egypt (about 1550 B. C.) alludes to hemorrhoids. The Hindus (about 1000 B. C.) had knowledge of hemorrhoids and five kinds of anal fistulas. In the Old Testament there are references to proctologic diseases.

We are on firmer ground with the Greek writers (about 400 B. C.), for in addition to their manuscripts some of the instruments actually used in the treatment of rectal disorders have been passed on to us. The diagnosis and treatment for anorectal fistulas is discussed in the Hippocratic writings. Celsus (first century A. D.), in his encyclopedic work, discussed the diagnosis and treatment of fistulas. Galen, who flourished in 165 A. D., had a theory that ascites could be caused by blood retained in hemorrhoids. Nothing further of importance to record can be found until the sixth century, when Aetius, physician to the Court of Constantinople, advised the actual cautery for procidentia recti, a procedure which under certain circumstances is still in use.

We now skip to the 14th century to the time of John Arderne, whose treatise on the cure of fistula embodied some major principles which still hold. Now, another skip to 1819, at which time a set of iron and bronze surgical instruments were unearthed in the long-buried city of Pompeii. Among them is a two-bladed speculum for anal and rectal examinations, a modification of which has its modern counterpart. The year 1835 is a memorable one in the history of proctology, for it was the year that Frederick Salmon of London founded St. Mark's Hospital for Fistula and Other Diseases of the Rectum. Later, also in London, the Gordon Hospital for Diseases of the Rectum was erected.

Early American Proctology

Joseph McDowell Mathews of Louisville, Ky., the 51st president of the American Medical Association, is referred to as the father of American proctology. Seventy-five years have elapsed since his decision to limit his practice to proctologic disorders, and he prepared himself for the specialty by visiting clinics and medical centers in New York and London. He spent considerable time at St. Mark's Hospital with the Allinghams and others.

After his return to the United States, after some cursory attempts, a meeting was called in 1899, largely through his efforts, for the purpose of organizing a society for those interested in this special branch of medicine. In that year and from that meeting the American Proctologic Society was founded. Mathews was its first presiding officer. Since then the Society has fluorished.

After four years of preliminaries, finally, in 1916, a Section on Proctology of the American Medical Association was organized and combined with the Section on Gastroenterology. The first session of the Section on Gastroenterology and Proctology of the American Medical Association was held in New York City in 1917, 42 years ago. These special fields of medicine have progressively developed through the untiring endeavors and zeal of its devoted leaders to whom the Section owes its success.

The proctologist or, if another name is preferred, the specialist in the diagnosis and treatment of colonic and anorectal diseases is a bipartite specialist, having both medical and surgical methods available, and for that reason is in an advantageous position to treat conditions such as chronic ulcerative colitis and decide promptly when medical treatment should be discontinued and surgery instituted, rather than permitting the disease to progress to a state of inoperability.

Actually some form of proctology is practiced by specialists in other fields, as well as by general practitioners. I am certain that recognized roentgenologists and dermatologists do not treat pruritus ani until and unless the causative factor or factors have been searched for, but there are persons whose office equipment includes x-ray machines who will treat that condition by radiation without the benefit of proper proctologic examination.

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As a proctologist I have found it profitable to attend selected sessions of the Sections on Anesthesiology, Dermatology, General and Abdominal Surgery, Pathology and Physiology, and Radiology of the Scientific Assemblies of the American Medical Association, as well as those of my state medical society. The truth of the matter is that, although specialists practice a limited branch of medicine, they do and should have overlapping knowledge of other departments of medicine. Disorders such as perianal melanoma, epidermoid (squamous cell) anal and perianal carcinoma, perianal warts, and allergic and fungoid conditions demand an interrelationship and interchange of information and ideas.

Physician First—Specialist Second

We should be physicians first and specialists second. There is a natural interrelationship among several specialties, and this relationship should be accepted amicably and with cooperation and not decried. I submit that pruritus ani not infrequently deserves and receives the benefit of dermatological, medical, and roentgenologic consultations, but no such case should be treated unless a proctologic survey has been completed.

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Because of the proximity of pilonidal disease to the anus, proctologists treat that condition, though it has no embryologic connection with the intestine. Perhaps it belongs in the realm of general or even orthopedic surgery, but advances reported in the treatment of pilonidal disease have emanated principally from proctologists who have devoted considerable study to the subject.

Proctologists are exposed to many incidences of regrettable complications due to inexpert therapy, and calling attention to such occurrences should not be cause for taking umbrage. Of course it may be stated that the proctologist sees only the poor results, but there should not be as many avoidable poor results as come to our attention. I hasten to emphasize that general surgeons properly trained in colonic surgery do excellent work in that category. But the modern proctologist emerges only after having had the benefit of adequate general, including a good measure of colonic, surgical training as well as specialized training in anorectal surgery, and he is a source of good proctologic practice for the community in which he chooses to locate. Wherever proctology is not practiced as a specialty, anorectal diseases and many aspects of colonic disorders assume a lesser position and often do not receive proper consideration and attention.

General surgeons or surgical specialists, including proctologists, may choose to perform some operations and not others. There are not now many surgeons who demand all surgery for their domain. Wherever such a person may exist he must be aware that in the performance of such an all-encompassing variety of operations, his effectiveness must be deficient and below standard in some fields.

As medicine advances and certain diseases are conquered, the need for a specialty may be obviated, or modification and revision of a specialty may become necessary. The introduction of revealing research findings may alter the entire conception and method of procedure toward a medical or surgical problem and thereby markedly affect a specialty. The discoveries in the modern treatment of tuberculosis, and the modern use of sulfonamides and antibiotics, are examples of the change that can be brought about by new findings. Specialties rise as their need arises and fall for lack of usefulness. But unless the practitioner is a "one disease specialist," specialization will continue to occupy a useful and necessary place in the practice of medicine.

As stated earlier, proctology means more than the treatment of hemorrhoids, fistulas, and pruritus ani. A visit to the proctologic clinic of an accredited hospital staffed by men who are well trained, expert, and dextrous will make the visitor realize that proctology is a much needed specialty. Only those unfamiliar with the activities in modern proctologic clinics believe differently. Many of our medical schools, recognizing the need for adequate proctologic instruction, have established divisions or departments of proctology, but there are some which style themselves great medical centers where only meager attention is paid to the teaching of proctology. Graduates of such schools become very conscious of what they missed in school when as interns they are given proctologic instruction.

Duties and Responsibilities

We of the medical profession, whether specialists or general practitioners, have a duty and responsibility to the individual men and women and their children who come or are brought to us in their time of need and anxiety. We should give attention to the personal and emotional requirements of these persons, as well as the scientific medical care which they seek. As physicians we must never forget that, whatever the region of our special interest, we are treating a person and not just a diseased part of that human being. We who are privileged to share the confidences of our patients must practice the art as well as the science of medicine and thus be of the most possible use to those who place their lives and trust in our hands. This can be done and is being done through the wholehearted collaboration between specialists and generalists who complement each other's efforts toward the promotion of the health and well-being of our fellow man.

80 Hanson Place (17).

INCOMPETENT OS OF THE CERVIX AS A CAUSE OF FETAL LOSS

E. Stewart Taylor, M.D.
and
Richard R. Hansen, M.D., Denver

The surgical procedure here described aims to prevent premature birth and fetal wastage caused by weakness of the musculature of the cervix uteri. The operation, devised by Shirodkar, consists of the application of a purse string or tourniquet to the cervix. It is indicated only for patients who have a history of repeated unexplained miscarriages during the second trimester and who demonstrate a progressive cervical effacement and dilatation between the 14th and 28th weeks of gestation. It was performed in 40 patients who had had 182 previous pregnancies with 20 premature and only 15 full-term infants surviving. Among the 40 patients after operation, only 8 had unsatisfactory results, for reasons here analyzed, while 32 delivered normal infants, including two sets of twins. Ten deliveries occurred per vaginam after removal of the purse string, and 22 were cesarean.

The incompetent internal os of the uterine cervix has been found to be a cause of premature termination of pregnancy between the 16th and 28th weeks of gestation. This condition occurs no more than once in 500 pregnancies, according to our experience at the Colorado General Hospital. We have, however, been able to collect data on 40 patients who have been surgically treated for an incompetent internal cervical os. The treatment was carried out during pregnancy in each instance. These patients and their management are the subject of this report. The patients in this group have been under the care of members of the department of obstetrics and gynecology and have been operated on in the past two years at Colorado General Hospital, Denver General Hospital, Fitzsimons Army Hospital, and private hospitals of this community. The operative procedure used is a modification of an operation originally suggested by Shirodkar [1] of India and introduced to the United States by Barter and associates.[2] In principle, the operation consists of a purse-string suture placed submucosally around the cervix at the level of the internal os in order to prevent expulsion of the fetus before maturity.

Lash,[3] in 1949, was the first person in the United States to focus attention on the incompetent cervix as a cause of abortion. He stated that the incompetent cervix was a result of trauma and that a defect could be found in the cervix. Since then the diagnosis of incompetent cervix has been made in women without a history of cervical trauma and without a recognized physical defect of the cervix. Palmer [4] postulated the congenital incompetent cervix and described a short weak cervix; he called the condition "hypoplasia of the cervix." Jeffcoate and Wilson [5] performed hysterographic studies on selected women whose obstetric histories were unknown to the radiologist. Of 31 women who had experienced normal labors at term, one had a funnel cervix and 5 had minor cornual malformations. Of 69 women who had experienced premature labor of unknown cause, 33 had a dilated internal os and 15 had cornual malformations. Barter and others [2] suggest erect posture of man as a factor in congenital incompetence. Baden [6] has discussed the physiological relative cervical incompetence in twin gestation.

Diagnosis

The diagnosis of the incompetent cervix is suspected through history of recurrent middle trimester fetal losses. There is usually a sudden painless passage of amniotic fluid between the 16th and 28th weeks of gestation followed by almost immediate expulsion of the conceptus.

In one-half of our patients, there was a history of previous gynecologic or obstetric trauma. Trauma may arise from a previous delivery, instrumental dilatation of the cervix, hysterotomy, or cervical amputation. A midforceps operation or a difficult breech extraction may cause damage to a cervix, with later incompetence. An apparently normal term delivery may rarely destroy the functional integrity of the cervix. A visible cervical laceration may cause cervical incompetence in subsequent pregnancies.

Presumptive evidence of cervical incompetence can be demonstrated by the painless passage of a 7-mm. Hegar dilator through the internal os of the cervix while the patient is not pregnant. Uterine anomalies such as a bicornuate uterus must be considered in the differential diagnosis of repeated abortions. Hysterographic confirmation of cervical incompetence is not necessary, but a hysterogram is valuable for the demonstration of abnormalities of the uterine body.

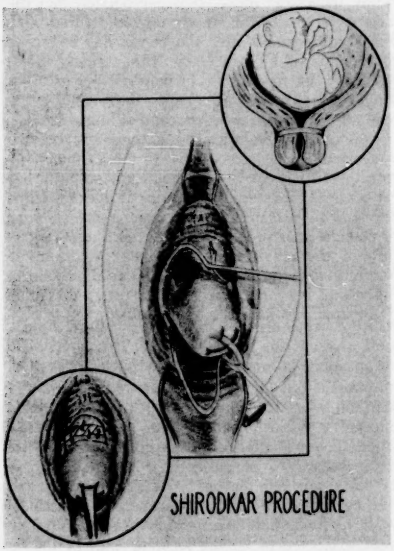
An important clinical test for the presumed incompetent cervix is careful observation of the cervix during pregnancy. The patient who has an incompetent cervix will demonstrate cervical effacement

From the Department of Obstetrics and Gynecology, University of Colorado Medical Center.

and dilatation starting between the 14th and 20th weeks of gestation. A suspected diagnosis is confirmed when the cervix begins to dilate and membranes can be observed or palpated in the cervical canal. The open cervix should be detected before the membranes prolapse into the vaginal vault. If prolapse of the membranes occurs, the intrauterine volume diminishes, with possible shearing of the placental bed, bleeding, and delivery of the immature fetus. In other instances, the exposed membranes become infected and rupture, and delivery occurs soon thereafter.

Treatment

Treatment of the incompetent cervix depends on the cause. If there is a history of previous midtrimester fetal loss, and a deep laceration of the cervical canal, this defect should be repaired by trachelorrhaphy when the patient is not pregnant. Any other procedure in these patients is likely to fail because the basic defect is not corrected. Two of our failures demonstrate the improper selection of operative procedures for the incompetent cervix.



Principles of Shirodkar procedure to correct incompetent internal os of cervix during pregnancy.

A purse-string suture around the internal os is not proper treatment for cervical incompetence secondary to a laceration of the cervix.

Shirodkar [1] has emphasized his observation that bed rest will often avert the premature labor in this syndrome. He sought a more certain method of reinforcement of the cervix. Shirodkar used a fascia lata transplant placed submucosally around the cervix as a tourniquet at the level of the internal os.

Indications and Contraindications.—The Shirodkar procedure is indicated only for patients who have a history of repeated unexplained midtrimester fetal loss and demonstrate a progressive cervical effacement and dilatation between the 14th and 28th weeks of gestation. Durfee [7] reported six consecutive failures to avert labor when a surgical procedure for closure of a partly dilated cervix was performed on patients as late as the 28th week of pregnancy.

TABLE 1.—*Successful Results of Treatment of the Incompetent Cervix*

	Previous Pregnancies			Cervix Closed by Operation	
Patient No.	Fetal Losses, No.	Term Deliveries, No.	Surviving Premature Infants, No.	Week of Gestation	Infant Weight, Gm.
1	7	0	0	21	2,780
2	7	0	0	26	2,430
3	1	0	3	24	2,400
4	6	0	0	15	2,740
5	2	1	0	25	2,600
6	1	0	0	18	*
7	2	0	0	19	*
8	2	0	0	21	2,640
9	5	0	0	18	2,700
10	5	1	1	18	3,240
11	5	0	0	15	2,770
12	4	0	1	16	3,100
13	1	1	3	23	3,040
14	5	0	0	20	2,880
15	6	0	0	14	2,760
16	2	0	0	20	2,580
17	3	0	0	16	3,200
18	4	1	4	30	1,900
19	2	0	0	25	3,400
20	2	2	3	27	4,000
21	3	1	0	22	3,480
22	5	0	1	22	2,000
23	1	0	0	20	1,900
24	3	4	0	23	3,400
25	5	0	0	23	3,400
26	3	0	0	16	3,060
27	3	1	0	12	2,650
28	2	0	2	16	3,280
29	3	1	0	23	3,500
30	2	0	0	19	3,210
31	10	0	0	14	3,290
32	6	0	0	13	3,100

* Twins.

Technique of Operation.—Our technique (see figure) is similar to that described by Barter and others.[2] The patient is given a general anesthetic for the operation. The anterior and posterior lips of the cervix are grasped with separate tenacula, and a 3-cm. transverse incision of the posterior vaginal mucosa is made at the level of the internal os. A similar anterior incision is made, and the bladder is dissected free from the cervix to the level of the internal os. An 8-mm. Mercilene tourniquet is then passed around the cervix at the level of the internal os, as demonstrated in the illustrations. This band is then tied as tightly as possible. Anchoring sutures of silk are then placed through the band and cervical fascia, anteriorly and posteriorly. The vaginal mucosa is closed with interrupted chromic catgut sutures.

The postoperative course is usually uncomplicated. The patient is able to leave the hospital on the fourth or fifth postoperative day. No progesterone or other hormone treatment is used. The patient should be cautioned to abstain from intercourse for three weeks. Normal household activities may be resumed one week after the operation.

Results

Our group of 40 patients had had 182 previous pregnancies with only 35 surviving infants, a reproductive efficiency of 19% (tables 1 and 2). More important is the fact that only 15 of the 35 surviving infants were at term when delivered. The term deliveries occurred as the first pregnancies experienced by these patients. A normal term delivery, therefore, seems to be followed by cervical incompetence in a rare instance. The other 20 surviving infants were born prematurely. Seven of these infants have permanent complications of prematurity, such as blindness and mental retardation.

TABLE 2.—*Failures in Treatment of the Incompetent Cervix*

Patient No.	Week of Gestation at Operation	Week of Abortion	Apparent Cause of Failure
33	16	21	Deep cervical laceration with protrusion of membranes; spontaneous rupture of membranes
34	22	22	Deep cervical laceration with protrusion of membranes; intrauterine fetal death
35	19	23	Abruptio placentae
36	26	27	Ruptured marginal sinus of placenta and delivery
37	25	27	Tourniquet slipped
38	14	22	Prolapsed membranes, intrauterine death
39	16	16	Spontaneous rupture of membranes
40	14	17	Spontaneous rupture of membranes

Thirty-two of the 40 patients who have had a Shirodkar operation performed during pregnancy have been delivered of normal infants. Our success rate is 80%. There has not been a failure in the last 16 operations performed. Two sets of twins were born to the successfully treated group. Twenty-two of the successful group were delivered by cesarean section, while 10 delivered vaginally after removal of the tourniquet.

There were eight failures in our series of 40 patients who were treated surgically during pregnancy after a diagnosis of cervical incompetence had been made (table 2). Two patients should not have had a band placed around their cervices because they had deep lacerations of the cervix that needed trachelorrhaphy. These patients have each since had a trachelorrhaphy. In two other instances, the cervix had been dilated widely before operation and the membranes were prolapsed through the cervix. Rupture of the membranes occurred a few days after the operation had been performed.

If a cesarean section is performed, the integrity of the cervix is conserved and future term pregnancies are probably assured. Three of our 40 patients are pregnant for the second time, and their pregnancies are progressing normally.

Comment

The type of suture material used for closure of the cervix has little effect on the final results. We have discontinued the use of homologous fascia lata transplants because of the problems secondary to obtaining fascia from the patient's thigh. We are currently using an 8-mm. single-thickness strip of Mercilene tape. Mercilene tape is strong and stimulates adequate fibrosis but causes very little other tissue reaction. It has an advantage in that the 8-mm. size cannot be tied too tightly about the cervix. The nonabsorbable tourniquet may be removed after termination of the pregnancy if abnormal tissue reaction results.

The incompetent cervical os is a positive entity for which a surgical treatment is available and effective in a high percentage of patients if the diagnosis is correct. There are certain patients who have such a prolonged history of midtrimester fetal losses that the diagnosis can be made practically by history alone. It is our opinion that the incompetent cervical os should be treated only during pregnancy, after the cervix has begun to show signs of incompetency. The patient who is suspected of having an incompetent cervical os should be examined frequently during her pregnancy for signs of early effacement and dilatation of the cervix. Dilatation of the cervix is gradual and usually is not perceptible to the examiner before the 14th week of pregnancy. It has been our experience, however, that wide dilatation of the cervix with prolapse of the membranes combine to make a poor prognosis even after operative closure of the cervix. It is necessary, therefore, to interfere with surgical closure before dilatation of the cervix has progressed beyond early dilatation if the best results are to be obtained.

Conclusions

Incompetence of the internal cervical os is an infrequent but important cause of midtrimester abortion. Surgical correction of the incompetent internal cervical os during the second trimester of pregnancy is attended by successful pregnancies in at least 80% of patients, if the patients are properly selected for operation. The operation is best performed not earlier than the 14th gestational week and not later than the 27th week. The patient suspected of having incompetency of the internal cervical os should be examined during pregnancy at weekly or biweekly intervals so that pathological and early effacement and dilatation of the cervix may be diagnosed. Surgical closure should be considered only after the internal os has started to dilate.

4200 E. Ninth St. (20) (Dr. Taylor).

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MEDICAL PRACTICE, MEDICAL CARE, AND MODERN SOCIETY

Malcolm S. M. Watts, M.D., San Francisco

Medical practice, public health, and social welfare have a common basic goal—to work for the best interest of the patient, the individual human being. This must always be clearly recognized by all concerned in their thinking and action. This goal finds its highest expression in terms of the golden rule. The medical care provided for others must be only that which one would wish to receive for oneself.

Problems in Providing Best Care

The problems of medical practice, medical care, and modern society bring us face to face with some of the most complex problems of our times. Perhaps some definitions are in order. First, who are those who provide this care and who are those who receive it? It is clear that the providers cannot be limited to doctors, nurses, medical technicians, health departments, and social welfare agencies. These groups do not supply the necessary funds. The providers, therefore, must also include those responsible for the source of funds, which in any scheme for medical care is ultimately the consumer or the public. In the final analysis this includes everyone. Every person must meet these costs out of his own pocket; through prepayment; by means of funds provided by industries, through increased cost of living; or directly or indirectly in taxes. It also follows that in these broad terms the recipients of medical care cannot be limited to those who are sick, injured, or maladjusted at any given moment but must include anyone who is or may become sick; this, too, includes everyone. Thus, in these social terms, those who are to provide the medical care and those who are to receive it are the same.

Assistant Dean, University of California, School of Medicine; Chairman, Public Relations Committee, California Medical Association.

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It is fallacious to consider medical care as a product or commodity, to assume that medicine has developed into a precise science, to think that medical care is not ultimately paid for by somebody, or to suppose that the interests of the community so nearly coincide with those of the individual person that he can be reduced to a file number without personalized care. There are many types of medical practice and many ways of financing the operation of hospitals and offices, the wages of personnel, and the costs of equipment and medicaments. The experience of the California Medical Association shows that it is possible to develop successful programs that will interfere but little with the traditional relationship between doctor and patient.

Therefore, it becomes of most practical importance to be careful to provide only that kind of medical care for others which one would wish to receive for oneself and one's family.

Just what are the essentials of this medical care which Americans, individually and collectively, must provide for themselves? A recent report [1] of a committee of the American Medical Association provides an answer. "Medical care is that service which uses every means available to secure and maintain a state of physical and mental well-being in the individual. Good quality medical care results from the full use by the physician of his art, skill and knowledge, and his utilization of the scientific facilities available to him. It depends upon the phy-

sician's sincere interest in the patient and the patient's faith in his physician." Thus, the essentials include the patient's needs, the physician's desire to help, the patient's belief that the physician can and will help, and the tool or technology by which the help is given.

It is often inferred that medical care is not now provided for all who need it. To any extent that this is true, it presents a serious problem to society and to the medical profession. However, it has long been a matter of pride to the medical profession that it, with the support of the community, has always seen to it that everyone receives basic necessary medical care regardless of ability to pay and that the standards of this care are as high as anywhere in the world. It would appear rather that present problems in medical care pertain to its rapidly increasing cost and complexity; changes in the social, economic, and political environment in which it must be rendered; and the need to insure that the best medical care is available to each individual in these changing circumstances. Fundamentally, this is of supreme interest to everyone, since, in social terms, the ultimate providers and the ultimate recipients are basically the same persons.

Some Causes

What lies behind these complex problems? The phenomenal growth of science and technology, particularly in the last 50 years, has had profound effects on medical care and has increased its complexity and cost. It has led to specialization which extends even beyond the medical profession and includes the work of many paramedical technologies and many public and voluntary health and welfare agencies. Further, this growth of science and technology has affected the whole of society and has served to bring everyone into closer and more interdependent relationship.

Profound economic changes have also occurred. The devaluation of the dollar together with rising taxes during the last 25 years have made it almost impossible for the average person to save adequately to meet the modern cost of serious illness. Techniques have therefore been developed to spread this cost more evenly throughout the population. These include prepaid funds for medical care, tax-free funds in the form of "fringe" benefits, and the use of tax funds themselves. These developments have produced complex changes in so-called traditional medical practice.

There have also been important social and political trends which are probably inherent in the evolution of our democracy. Over 100 years ago de Tocqueville predicted that in a democracy based on the principle of majority rule, the particular interests of the individual person would gradually become subservient to the principle to the greatest good for the greatest number. There is considerable evidence to suggest that this is in fact now occurring. Public officials increasingly rely on the advice, counsel, and financial support of organizations representing the special interests which large groups of persons have in common. Even the courts seem less apt to uphold the right of a person to be different. In passing, it is a curious paradox that "advances" in democracy tend toward compulsory collectivism while the collectivist states themselves have rediscovered that individual persons are not all alike and have found it necessary to reward individual initiative, responsibility, and accomplishment.

What bearing do these developments have on the medical care which everyone must provide for everyone who needs it? There has been much confusion. In the smoke, fire, and emotion that has been generated it is all too often forgotten that the goal is to do what is best for the patient and that the patient is an individual human being whose medical problems may be the same or different from those of his neighbors.

Some Fallacies

Several fallacious concepts have been introduced which have had surprisingly wide acceptance and therefore bear on the problem.

1. Many persons have come to consider medical care to be simply a product or commodity consisting of diagnostic procedures, x-rays, laboratory tests, operations, pills, injections, and the like. To them, the answer to any problem in medical care lies merely in applying well-known mass production and mass distribution techniques to this commodity in the good old American tradition.

2. Others have come to believe that medical care is in fact a precise science, which could almost guarantee health for all if it could only be made available to everyone. This fallacy is also obvious. Medical science is by no means developed to this point, but even if it were precise, the patient is not, and therefore medical care can never be. This fallacy is perilously close to that of the hopeless search of Ponce de Leon for the fountain of youth.

3. Economic developments also have led to curiously unclear thinking. It is believed by many that medical care should be "free." The fallacy here is obvious. It must ultimately be paid for by the ultimate consumer—the patient. The more complex the system the more costly it becomes, because the costs of the system must be added to the costs of patient care. Also, it is often assumed the doctor will work devotedly in the interest of his patient no matter who pays him. This somehow assumes that doctors are different from other persons, and this is not true. To the extent that a union doctor works for the union, a government doctor works for the government, an insurance doctor works for the insurance company, or a doctor works for a closed panel, a group, or a clinic, his interest in the patient is proportionately reduced. As a corollary to this, when pools of money for medical care are collected through prepayment, fringe benefits, or

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tax funds, the question is seldom asked "whose money is it?" Such funds are rarely handled as though they belonged to the patient. This has far-reaching implications in terms of who is working for whom, the special interests of so-called third parties who operate the funds, and the personal interests of the patient whose ailments may be no one's business but his own.

4. The principle of the greatest good for the greatest number and its development in our democracy has been mentioned. Under what circumstances does this principle apply in the best interest of the individual patient? On reflection, it would appear that it applies whenever there is, or may be, a great disparity between the numbers of persons in need of medical care and the amount of services which may be available. Thus, it has been found to apply in potentially epidemic situations such as when the public health is endangered, in military medicine, in civil defense, and also in certain remote or economically backward areas where adequate facilities and services are not available. But the principle of the greatest good for the greatest number has not been found appropriate to the best medical care for the individual patient in the normal circumstances of American life. The average American has received and continues to be entitled to personalized care for his individual needs which may or may not be similar to the problems of others. This best medical care is and should continue to be the goal and purpose. The individual human being should not be reduced to the status of a statistic or a file number and receive his medical care as a statistical probability.

5. Reference has been made to some political trends in the evolution of democracy. The fundamental question here appears to be "To what extent is 'freedom to' to be sacrificed for 'freedom from'?", i. e., "To what extent is the independence of the individual and his right to personal consideration to be sacrificed to dependence on and interdependence with the greatest good for the greatest number?" Medical care is now considered a social necessity along with food, shelter, and clothing. But so far, no one in America has seriously proposed that a person's right to choose his food, shelter, or clothing be curtailed. The community has always provided the essentials for those who were unable to afford the basic necessities. Perhaps it is as fallacious to compel a person to sacrifice his freedom to have the medical care he chooses as it is to expect him to sacrifice his freedom to choose his food, his housing, and his clothing. In this sense, medical care problems are fundamental to individual freedom in the American way of life.

If it is agreed that only the best in medical care can be satisfactory for Americans, then medical care must be personalized and individualized and the dignity of the human being maintained. Anything less is acceptable only as a stop-gap emergency measure. The patient's special and particular needs for medical care must be recognized, diagnosed, and treated by a doctor whose primary interest and obligation is the health and welfare of his individual patients. Tools and technology must be available economically and otherwise. The element of the patient's belief that the physician can and will help with his problem must be preserved. Somehow, these essentials of the best medical care must remain realities in the new technological, economic, and social environment.

The Experimental Approach

The medical profession is an old profession. It knows the meaning of truth. It knows that, if something was really true yesterday, it is true today and will still be true tomorrow. It knows that these essentials of medical care are such truths and that they must somehow be preserved in the interest of the patient if the true goal of the best medical care for all is to be achieved. In the historical development of its science and technology, medicine has dealt with many complex problems. It has tested and applied old truths in many new situations. In its research it has explored many blind alleys. It has seen many promising drugs, operations, or "cures" proved dangerous or worthless. It has always been willing to experiment but never when the risk to the patient seemed undesirable. But many of its experiments have been productive of new knowledge and useful techniques. It has always been willing and able to move rapidly and effectively whenever a new treatment or a new method would clearly improve patient care.

It is these same traditional and sound principles which can and should now be applied to the political, social, and economic problems of medical care. Historically, the medical profession has served under every kind of political, social, and economic system. It has considerable experience. Its goal continues to be the best medical care for the patient. It has opposed social and political experiments which it believed to be not in the best interests of the patient in the same way that it refrains from scientific experiments which carry an undue risk for a human being. It shies away from experiments which may or may not work but from which there can be no easy retreat; but it has not remained aloof from these problems; as they have become clarified and defined, the profession has carried on research. It has conducted experiments and encouraged others to do the same thing so long as the best quality in medical care for the patient was not jeopardized. There are others, mostly outside the profession, who shortsightedly have been more concerned with quantity in situations where quality should be their true goal.

There are many types of medical practice. These include traditional solo practice with the use of consultant specialists when necessary; partnerships where doctors of the same specialties are able to exchange their knowledge and experience and yet

maintain a close relationship between doctor and patient; group practice where small or large groups of doctors, usually of different specialties, band together and where at times the interests of the group of doctors may tend to supersede the interests of the patient; various forms of panel practice where patients in a given medical care program must see certain doctors in order to gain the benefits of the program and where the doctor is often more responsive to the interests of the program than of the patient; insurance medicine where the doctor works for the insurance company; or government medicine where the doctor is clearly working for the government.

There are many types of medical care plans which provide varying degrees of coverage for hospital, home, office, and outpatient care; professional services; diagnostic laboratory and x-ray services; and medicaments. Other plans provide for care in clinics, clinics associated with particular hospitals, plan-operated health centers, and the like. To be satisfactory to the purchasers these plans require some degree of certainty of coverage. To be satisfactory to the administrator there must be some predictability and control of costs. To be satisfactory to the patient they should provide freedom of choice and freedom of action to both doctor and patient in the management of the patient's particular problem. In general, the more complex the program, the more the costs are increased by administrative overhead, the more the physician's effort becomes circumscribed by administrative regulation and red tape, and the more the special interest of the patient becomes subservient to the collective system.

It is not possible here to assess these medical practices and medical care plans in terms of (1) the essential elements of the best medical practice, (2) the various fallacies which seem to creep into thinking about medical care, (3) problems of abuse, administrative waste, and overhead, and (4) the ultimate costs which must be met by the individual consumer, the patient or the potential patient. It appears that to date no medical care program or system of medical practice, including traditional medicine, has been developed or proposed which entirely meets all of the desirable criteria.

In California the medical profession has taken three major experimental steps toward the solution of some of these problems. About 20 years ago it established the California Physicians' Service (Blue Shield), which was one of the earliest experiments in prepayment for hospital and physicians' services. The experience of the California Physicians' Service has been a stimulus and a guide to many other programs. In an effort to help meet the crucial problems of predictability in physician fees, the California Medical Association has carried out the Relative Value Fee Study which relates doctors' fees for various services as to one another. This study has been of fundamental importance and has made available a guide to insuring agencies for estimating doctors' usual fees for various procedures and services in various parts of the state.

San Joaquin County in California has developed what is known as the Foundation Plan for Medical Care. This has been in operation for only a little more than two years. In this program the members of the county medical association may join the foundation and agree to accept a fee based on the Relative Value Fee Study and local costs with reductions in fees for those in low income brackets. This enables the foundation in turn to contract with groups of patients for their professional care. In this program hospital care, laboratory diagnostic precedures, and medicaments are separately insured through Blue Cross, Blue Shield, or a private insurance carrier. This program interferes little with the traditional relationship between doctor and patient and with the best medical care for the patient, because the foundation includes most of the doctors practicing in the area and it provides what appears to be a workable solution for many economic and social needs.

Comment

The problems of medical practice, medical care, and modern society are in somewhat a state of turmoil. One is reminded of a boat running through a rapids. The boat is traditional medical practice. It contains the gear essential to the best care for the patient. There is no turning back. The boat must be kept upright and kept pointed toward the goal in spite of buffeting from many sides. One must keep the essential gear from falling out and too much water from splashing in. The goal, the end of the rapids, is to preserve the dignity of the patient in the personal matter of his health, to strengthen the quality of his medical care, and to adapt these fundamentals to the social, political, and economic needs of the environment.

Finally, it has been said that we are engaged in a great experiment in democracy and that it is by no means proved yet that the experiment is a success. In its concern with the welfare of its patients, traditional medicine is dedicated to making this experiment a success. It will continue to work for the best interest of the patient, who is identical in social terms with the individual human being—that often forgotten element in democracy. In this sense, the providers and the recipients of medical care are all in the same boat and are all having an exciting trip down the rapids. When the solutions to these complex problems become clear, traditional medicine will act promptly and effectively in the interest of the patient as it has always done.

909 Hyde St. (9).

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LISTERIOSIS—SUMMARY OF SEVEN CASES OF LISTERIA MENINGITIS

Herbert J. Welshimer, Ph.D.
and
Nancy G. Winglewish, B.S., Richmond, Va.

The identification of Listeria monocytogenes as a cause of bacterial meningitis often has been missed due to its morphologic similarity to nonpathogenic diphtheroids. This gram-positive-staining micro-organism was seen in the spinal fluid specimens from two of seven patients. Specific identification was made by colony study on cultures grown from spinal fluid samples of each of the seven patients. The leukocyte count in the spinal fluid was not of diagnostic value. The signs and symptoms of the three infants and four adults did not differ from those of meningitis due to other agents. This organism also causes granulomatosis of the fetus and newborn infant, conjunctivitis, urethritis, and a type of infectious mononucleosis.

Most textbooks of microbiology restrict the discussion of the bacterium Listeria monocytogenes to a few sentences or paragraphs. Such presentations lead the reader to conclude that L. monocytogenes is of little moment to the clinician. The evidence of the past few years indicates that this organism, which produces a serious meningitis in persons of all ages or fatal granulomatosis in the fetus and newborn infant, is widespread but unrecognized.

The organism was isolated by Murray and associates [1] during an epizootic in the laboratory colony of rabbits and guinea pigs at Cambridge University during the years 1923-1924. Listeria infections subsequently became established in veterinary medicine with the discovery of a variety of clinical conditions occurring in domestic animals. The infection was not recognized in humans until 1932, when the Danish investigator Nyfeldt [2] isolated the organism from patients with an infectious mononucleosis syndrome. Several years later, workers in the United States reported isolating L. monocytogenes from patients with meningitis.[3] Scattered case reports of Listeria infections in humans were published, totaling 70 cases by 1949. As a result of the studies and efforts of Dr. Heinz Seeliger, of Bonn, West Germany, and Dr. G. Potel, of Halle, East Germany, many cases of listeriosis in humans have been discovered in Germany and interest in listeriosis has mounted. Seeliger [4] lists over 200 cases of listeriosis in humans that were reported during the interval from 1950 to 1955. One index of the increased frequency of isolation of Listeria in the United States is the fact that 22 cultures were submitted to the Communicable Disease Center in Chamblee, Ga., during the five-year period from 1949 through 1954, whereas in the next three years 66 cultures were received.[5]

It is interesting that persons who have become aware of L. monocytogenes after having recognized one case of listeriosis frequently observe other cases; consequently, there are a number of reports of two or more infections observed by the same worker. Hood [6] reported 10 cases of listeriosis occurring in the New Orleans area from November, 1954, to November, 1956. By the time of publication of her article, six additional cases had been diagnosed. Dedrick [7] published a report of eight cases of Listeria meningitis that appeared in and around Los Angeles from 1952 to 1956. She since has verified an additional case. Our experience may be the reverse of other laboratories, in that we became interested in the organism before any recorded appearance of human infections in our area. Only a month after we began our studies, an organism which we identified as L. monocytogenes was isolated from a patient with meningitis. There were no further isolations of Listeria from patients until over a year later. In the next 13 months, however, L. monocytogenes was isolated from the spinal fluid of six patients; indeed, two of these patients were admitted to the same hospital within the same week.

Murray,[8] Seeliger,[4] and Hoeprich [9] have given ample descriptions listing the manifestations of listeriosis, which include meningitis, granulomatosis of the fetus and newborn infant, conjunctivitis, endocarditis, urethritis, and a type of infectious mononucleosis. Meningitis is the predominant form of listeriosis in humans both here and abroad. Fetal and neonatal granulomatosis, which accounts for a high percentage of the Listeria infections abroad, has been observed only a few times in the United States and Canada.

Summary of Cases

The table presents details of the seven cases of listeriosis that were observed in Richmond. In all of these cases small gram-positive diphtheroids were cultured from the spinal fluid and sent to us for identification. In two of these cases resident staff members performed direct examination of the spi-

From the Department of Microbiology, Medical College of Virginia.

nal fluid by stained smears; the organisms observed were thought to be Diplococcus pneumoniae in one instance and "cocci" in the other. L. monocytogenes as seen in direct smears of spinal fluid frequently are more coccoid than bacillary in morphology and have been erroneously identified as cocci. Relative to the coccoid appearance, some workers have stated, "Very likely many cases of so-called sulfa- and penicillin-resistant pneumococcus meningitis (with the diagnosis based only on smears) are actually cases of unrecognized listeriosis. As a matter of fact, practically no case of chemotherapy resistant pneumococcus meningitis has been reported in Germany since 1951, and the number of cases due to Listeria is still increasing." [10] Easy decolorization of the organism in spinal fluid has led to presumptive diagnosis of Hemophilus influenzae [11] in gram-stained smears.

Blood cultures were negative in all but one patient (case 6; see table), a 14-day-old boy. The organism isolated from the blood was L. monocytogenes.

volvement was also reported by Dedrick [7] in her observations of listeriosis. One can only speculate as to the relation of these findings to the initial focus of infection. The usual routine bacteriological procedures for handling nose and throat specimens probably would fail to draw attention to L. monocytogenes unless it was present in abundance, in which case it most likely would be dismissed as a nonpathogenic diphtheroid.

As the organisms were isolated, in vitro sensitivity tests were performed with use of commercial antibiotic disks of the following strengths: chloramphenicol, 3 mcg.; tetracycline, 30 mcg.; erythromycin, 2 mcg.; penicillin, 2 units; and dihydrostreptomycin, 10 mcg. All seven strains of Listeria were found to be sensitive to these antibiotics. Penicillin was administered in all cases together with chloramphenicol or a sulfonamide, usually sulfadiazine. The patients, with the exception of two (cases 4 and 6) who died soon after admission, became afebrile within three or four days after chemotherapy was instituted.

Summary of Data from Seven Cases of Listeriosis

Case No.	Antigenic Type Isolated	Age, Yr.	Sex	Date of Onset	Date of Admission	Symptoms on Admission	WBC in Spinal Fluid		Therapy	Outcome
							Total	% Polymorphonuclear		
1.....	1	47	M	8/ 6/56	8/ 7/56	Stiff neck, fever, disorientation	580	20	Penicillin, sulfadiazine	Discharged well 8/28/56
2.....	4	57	M	12/ 8/57	12/ 9/57	Stiff neck, fever, vomiting, irritability	1,020	58	Chloramphenicol, penicillin	Discharged well 1/15/58
3.....	4	57	M	2/17/58	2/17/58	Comatose, fever, stiff neck	980	80	Chloramphenicol, penicillin	Discharged with residual brain damage 3/14/58
4.....	4	9 days	F	4/26/58	4/27/58	Tremor, fever, irritability	...	...	Chloramphenicol, penicillin	Died 4/28/58
5.....	4	10 mo.	M	10/ 2/58	10/ 7/58	Convulsions, fever, stiff neck	1,250	63	Chloramphenicol, penicillin, sulfadiazine	Discharged well 10/31/58
6.....	4	2 wk.	M	10/ 6/58	10/ 8/58	Convulsions, fever	2,409	20	Penicillin, sulfisoxazole, chloramphenicol	Died 10/11/58
7.....	1?	64	M	12/ 2/58	12/ 4/58	Disorientation, stiff neck, fever	143	13	Penicillin, sulfadiazine	Discharged well 12/18/58

The onset, in most instances, was characterized by lethargy, anorexia, and fever followed by the rapid development of neurological symptoms for which hospitalization was sought. One patient (case 7) presented influenza-like symptoms for a period of four days. He seemed to have recovered for two days and then relapsed. Two days after the relapse he was sent to the hospital. Another patient (case 5), a 10-month-old boy, exhibited fever and anorexia for five days prior to admission. The onset of symptoms in the other patients was sudden; it preceded the hospital admission by two days in one patient and one day or less in four patients.

Some upper respiratory involvement was indicated in three of the patients: The 47-year-old man (case 1) displayed some inflammation of the pharynx. The 10-month-old boy (case 5) had a purulent nasal discharge, a slightly injected pharynx, and slightly injected nonbulging tympanic membranes. The tympanic membranes of the 9-day-old girl (case 4) were red, with questionable bulging, and the pharynx was inflamed. Upper respiratory in-

Serums were obtained from five of the patients at various stages of their illness and were tested for Listeria antibodies by agglutination, hemagglutination, and complement-fixation tests. No significant antibody content was detected in any of the serums. This failure to detect antibody supports Hoeprich's [9] statement, "It is a peculiarity of Listeria meningitis that recovery has not been regularly associated with demonstrable humoral antibody." Perhaps successful chemotherapy reduces the number of Listeria so rapidly as to render the antigen level unsatisfactory for significant antibody response.

The possibility of in utero transmission was considered in the cases of the two babies who died. One, a 9-day-old girl (case 4), weighing 3,430 Gm. (7 lb., 9 oz.) at birth, was delivered at full term by a midwife. The mother's prenatal course was uncomplicated. The child, one of three siblings, was progressing nicely until she began refusing formula and developed a marked tremor of the hands. On examination at hospital admission a day later, rigidity of the arms and legs was noted, with con-

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stant hyperextension of the neck and back. The temperature was 102 F (38.9 C). The child was to be given 8 million units of penicillin and 0.5 Gm. of chloramphenicol over the next 24 hours; however, she died the morning after admission. Permission for postmortem examination was not granted. Serum obtained from the mother three weeks after birth of the child was examined for Listeria antibodies by agglutination, complement-fixation, precipitin, and hemagglutination tests; antibodies were not demonstrated by any of these tests. Others have detected antibodies in mothers who have delivered infected babies. The absence of maternal antibodies, and the fact that the baby was well developed and apparently healthy, leads us to conclude that the infection was contracted after birth and not in utero. The nature of the source of infection remains undetermined.

The other baby (case 6) was a boy, 2 weeks old at the time of admission. He weighed 2,948 Gm. (6 lb., 8 oz.) at delivery by a midwife, apparently without difficulty, and use of an evaporated milk formula was started. Two days before admission to the hospital he was seen by a public health nurse when he was exhibiting seizures of a grand mal type. His mother was reported to have had epileptic seizures for many years. At the time of admission there was slight nuchal rigidity. Spinal fluid taken on admission revealed 2,400 leukocytes, with 20% polymorphonuclear cells and 80% lymphocytes. Intravenous therapy with penicillin, sulfisoxazole (Gantrisin), and chloramphenicol was attempted; seizures continued, however, and the baby died two days after admission. Permission for autopsy was not granted. Serologic examination of the mother was not performed. It is possible that this baby was infected in utero at the terminal stages of pregnancy and escaped the lethal granulomatosis reaction that is the fate of the younger and less resistant fetus.

We have examined the meconium of over 170 aborted fetuses and babies that died shortly after birth, and neither direct microscopic examination nor culture has revealed Listeria in any of our specimens.

Epidemiology

There is no indication of a common source of infection among these seven persons. Two (cases 1 and 3) lived two city blocks apart; however, they were infected with Listeria strains of different serologic types. They may have been infected from similar sources but not the same source; furthermore, there was an interval of 18 months between their illnesses.

Two patients (cases 2 and 7) lived in the same general area, but they too were infected with different serologic types and their illnesses were about a year apart. One of these men (case 2) had been deer hunting regularly up until the day before his admission to the hospital. His history revealed that he had been bitten by ticks while hunting. He and his hunting companions were impressed with the number of ticks observed both on themselves and on the deer that season. One of the hunters provided one of us (H. J. W.) with several similar ticks, which tentatively were identified as Ixodes scapularis. This is of special interest because Gray,[13] at a recent symposium on listeriosis, stated that a Russian worker reported isolating L. monocytogenes from the Old World tick Ixodes ricinus taken from cattle. Gray mentions one other report of isolation of Listeria from an insect; namely, larvae of the fly Oestrus ovis, infesting the nostrils of listeriotic sheep in New Zealand. The possibility of insect transmission of listeriosis has not received much attention; we hope to conduct studies on transmission of listeriosis by ticks.

Of the seven strains of Listeria, we tentatively have identified five strains as serologic type 4 (since confirmed by Seeliger as belonging to the subtype 4b) and one strain as type 1. The organism from one patient (case 7) is a questionable type 1 strain. The frequency of occurrence of these types is in keeping with the observations of King and Seeliger,[5] who reported that 71% of their 100 United States strains were type 4b. They isolated only one type 3 strain and no type 2 strain. Only one type 2 strain has ever been isolated and identified, that being in Scotland.

Bacteriology

L. monocytogenes is a nonsporulating, gram-positive rod, about 0.5 μ in thickness and 1 to 2 μ in length. It is aerobic, facultative, and grows over a wide range of temperatures from 4 C to 42 C, with optimal growth at 25 C to 37 C. As mentioned previously, the organism may appear coccoid in spinal fluid; however, on subculture diphtheroid morphology is assumed, with a tendency toward pallisade formation. The failure to recognize L. monocytogenes can be attributed to its morphology, which is similar to that of the nonpathogenic diphtheroids that are commonly observed in clinical specimens. The usual procedure is to regard most diphtheroids as superficial contaminants of no significance. Any diphtheroid isolated from spinal fluid should be considered L. monocytogenes until proved otherwise.

The procedure which we have used to identify Listeria is as follows: The questionable diphtheroid is transferred to brain heart infusion broth and held at 23 to 25 C; at the same time the organism is streaked on plates of tryptose blood agar base to which 1% dextrose has been added. After 18 hours' incubation the brain heart infusion broth is observed microscopically in a hanging drop preparation. L. monocytogenes is unmistakably (although not violently) motile. This feature sets it apart from most diphtheroids. At higher temperatures the or-

ganism loses its motility in a few hours. The plates are incubated at 37 C for 24 hours. They then are examined under a stereoscopic microscope illuminated with the oblique lighting technique described by Gray,[13] who observed that such illumination produces a characteristic blue fluorescence that is distinctive, although the plate may be crowded with colonies of other organisms. The blue colonies are picked and a Gram stain is prepared to check morphology. At 24 hours the colonies are 0.5 mm. or less in diameter and are transparent and convex. A characteristic buttery odor is produced by the growth on the tryptose dextrose medium. The combined findings, motility and blue colony appearance, are excellent presumptive evidence that the diphtheroid in question is L. monocytogenes.

The growth from the plate is suspended in saline solution and a spot agglutination test is performed with antiserums developed in rabbits against different antigenic types of Listeria. A more thorough antigenic study is subsequently performed by preparing H and O antigen suspensions which then are tested with specific absorbed H and O antiserums.

Carbohydrate reactions are performed in meat extract peptone broth containing 1% of the test sugar. Esculin, dextrose, salicin, and rhamnose all are fermented in 24 hours at 37 C. The fermentation of these sugars serves to differentiate L. monocytogenes from Corynebacterium species with which it may be confused.[14] Listeria strains vary in their ability to produce acid in lactose and rarely produce acid in mannitol. Four of the strains we isolated fermented lactose after 96 hours' incubation; none fermented mannitol.

Since the organisms usually are noted first on blood agar, it should be mentioned that L. monocytogenes often produces a beta type of hemolysis around the colony. This should not be used as a criterion for differentiation of Listeria from other diphtheroids, because the hemolytic activity may be extremely weak or absent.

The production of a purulent conjunctivitis, usually accompanied by keratitis, is produced in rabbits by swabbing the everted eyelid with a young broth culture of Listeria. This is highly specific and can be used for confirmation of identity; however, we feel that the procedures mentioned above are sufficient in most instances.

Comment

As indicated above, the failure to recognize L. monocytogenes probably is primarily due to its morphology, which causes it to be disregarded in the belief that it is a diphtheroid skin contaminant. In our own experience we feel that the screening of diphtheroids has been adequate; however, the probability is great that there were at least as many unrecognized cases of Listeria meningitis as there were cases in which the organism was isolated. This presumption is based on the fact that the Listeria organisms, although easily grown, in some instances may be difficult to isolate. This is exemplified in the findings of Gray and others,[15] who observed cattle suffering with brain damage that was clinically diagnosed as listeriosis. Initial cultures of the macerated brain tissue of the infected animals were negative; after the tissue was held at 4 C for a period of three weeks to three months and again cultured, however, many Listeria colonies appeared. The low-temperature incubation of spinal fluid taken from patients with meningitis of undetermined etiology might well establish some of the cases of cryptogenic meningitis as Listeria meningitis.

Summary

Seven cases of Listeria meningitis were observed in Richmond hospitals over a 2¼-year period, with six of these cases appearing in the last 13 months of the study. Two of these patients (one 9 and one 14 days old) died.

All of the patients received penicillin and at least one other chemotherapeutic agent, either chloramphenicol or a sulfonamide. All seven strains of the organism were found to be sensitive to the five antibiotics with which they were tested in vitro. Two antigenic types of Listeria were isolated.

1200 E. Broad St. (Dr. Welshimer).

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DIAGNOSTIC ERRORS DUE TO FIXED ACUTE ECG PATTERN AFTER MYOCARDIAL INFARCTION

Harris Blinder, M.D.
and
Raanan Smelin, M.D., New York

Q waves and elevated S-T segments in the precordial leads of the electrocardiogram are commonly interpreted as indicating recent myocardial infarction. In the five cases here described they were so interpreted until evidence was obtained showing that the abnormalities had existed for periods ranging from three months to perhaps eight years. The patients were four men (aged 58, 67, 67, and 69) and one woman (aged 63). Aneurysm of the left ventricle was demonstrated in two of the five patients; in one the wall of the aneurysm was calcified. The erroneous diagnosis of recent infarction resulted in prolonged, unnecessary hospitalization in all cases and to the postponement of necessary surgery on three occasions. A single electrocardiogram is not sufficient to establish the diagnosis of recent myocardial infarction because the finding of Q waves and elevated S-T segments in the precordial leads after infarction sometimes persists indefinitely.

After myocardial infarction, the electrocardiographic pattern of the acute process, with elevation of the S-T segments, may persist indefinitely in some patients. This has been termed the fixed acute ECG pattern. In these patients electrocardiograms taken months or years after the acute episode may be misinterpreted as indicating a fresh infarction. In such cases, tracings taken because of anginal syndrome or congestive heart failure as well as routine preoperative or preemployment ECG's may lead to an erroneous diagnosis of acute myocardial infarction resulting in needless or unnecessarily prolonged hospitalization.

In this paper five cases are described in which such an erroneous diagnosis was made because of the persistence of the fixed acute ECG pattern. One of these patients (case 1) was hospitalized unnecessarily after a preemployment ECG; in three cases there was needless prolongation of hospital stay (case 3, three times), and in two cases indicated surgery was unnecessarily postponed. Aneurysm of the left ventricle was demonstrated in two of the patients by roentgenogram or fluoroscopy; the patient in case 2 revealed calcification of the wall of the aneurysm 14 years after the original infarction.

Report of Cases

CASE 1.—A 58-year-old man with no history of previous heart disease had an ECG (fig. 1, *top*) taken as part of a routine preemployment examination on Nov. 14, 1956. Because of the abnormal electrocardiographic findings (Q waves and elevated S-T segment in the precordial leads), the patient was hospitalized on an emergency basis, with a diagnosis of acute anterior wall myocardial infarction. Despite the absence of chest pain, abnormal physical findings, fever, or leukocytosis, the patient's condition was maintained with bed rest for four weeks. An ECG at time of discharge (fig. 1, *center*) revealed no significant change from the

From the Cardiovascular Service, Morrisania City Hospital.

admission tracing. A follow-up ECG taken three months later (fig. 1, *bottom*) revealed persistent elevation of S-T segments. It was then apparent that the patient had not suffered an acute myocardial infarction at the time of admission but had a fixed acute ECG pattern resulting from an undiagnosed infarction in the past. It was realized that the prolonged hospitalization described above had been unnecessary.

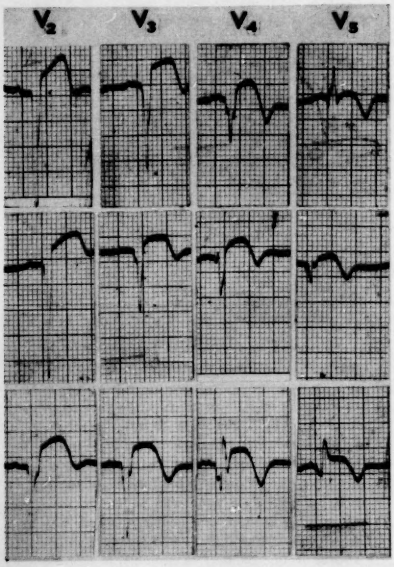

Fig. 1 (case 1).—Fixed acute ECG pattern for four-month period (*top to bottom*, Nov. 14, 1956; Jan. 2, 1957; and Feb. 7, 1957).

CASE 2.—A 63-year-old woman was hospitalized on Dec. 2, 1955, because of sudden onset of dyspnea. There was a history of myocardial infarction 14 years previously. Physical examination was unremarkable except for rales and rhonchi throughout both lungs. An ECG taken on admission (fig. 2, *top*) revealed elevated S-T segments and Q waves in the precordial leads. Despite the absence of chest pain, fever, hypotension, leukocytosis, or increased sedimentation rate, a diagnosis of acute anterior wall myocardial infarction was made, primarily on the basis of the electrocardiographic findings. No serial changes were noted in tracings taken two and six weeks (fig. 2, *center*) after admission (persistence of elevated S-T segments). A roentgenogram of the chest taken six weeks after admission revealed enlargement of the left ventricle with calcification of its left lateral wall (fig. 3). It then became apparent that the patient had not suffered an acute infarction, and the final diagnosis was aneurysm of the left ventricle with calcification of its wall. It was realized that the six weeks of hospitalization had been unnecessary.

The patient was readmitted to the hospital on March 1, 1956, during an attack of acute pulmonary edema. A diagnosis of acute infarction was made on the basis of an ECG taken on admission (fig. 2, *bottom*), which revealed elevated S-T segments and Q waves in the precordial leads. However, subsequent comparison with ECG's of Dec. 2, 1955 (fig. 2, *top*) revealed a fixed acute ECG pattern (persistence of elevated S-T segments). It was then realized that the diagnosis of fresh infarction was erroneous, and in several days the patient was discharged as improved with a diagnosis of aneurysm of the left ventricle.

CASE 3.—A 67-year-old man was hospitalized on Dec. 10, 1948, complaining of severe substernal pain. Physical examination was unremarkable except for distant heart sounds. An ECG taken on admission (fig. 4, *top*) was interpreted as indicating an acute anterior wall infarction. The temperature rose on the day after admission and remained elevated for two days. The patient was kept at bed rest and was discharged after four weeks with a diagnosis of acute myocardial infarction.

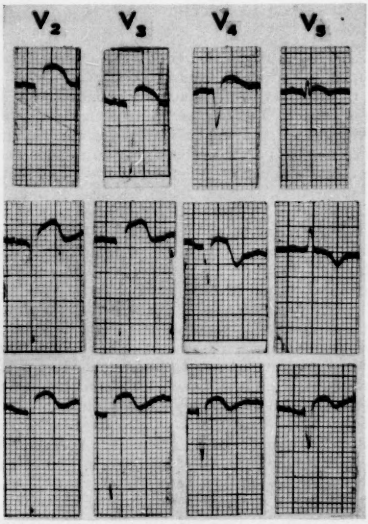

Fig. 2 (case 2).—Fixed acute ECG pattern for five-month period (*top to bottom*, Oct. 2, 1955; Nov. 16, 1955; and March 1, 1956).

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The second admission was on April 10, 1953, because of urinary retention, and prostatectomy was considered necessary. An ECG on April 14 (fig. 4, *center*) was interpreted as indicating an acute myocardial infarction, and therefore the patient was kept at bed rest for one month. Surgical treatment of the prostatic hypertrophy was postponed because of the diagnosis of acute infarction.

The third admission was on Aug. 17, 1955, to the genitourinary service because of acute urinary retention. A cystotomy was performed on Aug. 18. A routine ECG taken on Aug. 22 (fig. 4, *bottom*) was interpreted as indicating acute anterior wall myocardial infarction, and because of this a second-stage prostatectomy was delayed until Oct. 14, two months after the first stage. The patient was discharged on Nov. 7.

The fourth admission was on Oct. 13, 1956, because of cough, fever, and chest pain. The initial clinical diagnosis was pneumonia. An ECG (fig. 4, *bottom*) taken on admission was interpreted as indicating an acute myocardial infarction. However, comparison with previous ECG's taken as far back as Dec. 10, 1948, revealed a fixed acute ECG

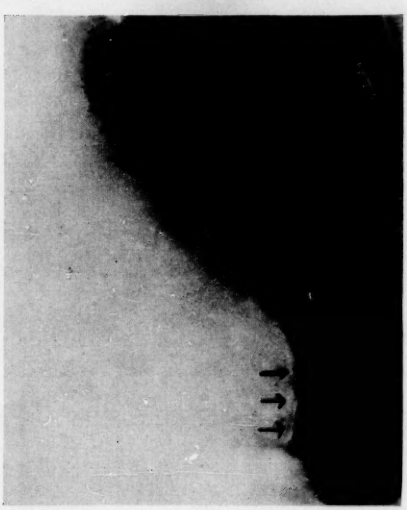

Fig. 3 (case 2).—Roentgenogram of left cardiac border, revealing calcification of aneurysm of left ventricle.

pattern (persistence of elevated S-T segments). It was then realized that the diagnosis of acute myocardial infarction made on the second, third, and fourth admissions were erroneous and that the prolonged periods of hospitalization and the delays in surgery at the second and third admissions had been unnecessary.

Case 4.—During cystoscopy for hematuria on March 20, 1957, a 69-year-old man suddenly complained of dyspnea and chest oppression, persisting for about 15 minutes. An ECG taken within one hour (fig. 5, *top*) was interpreted as indicating an

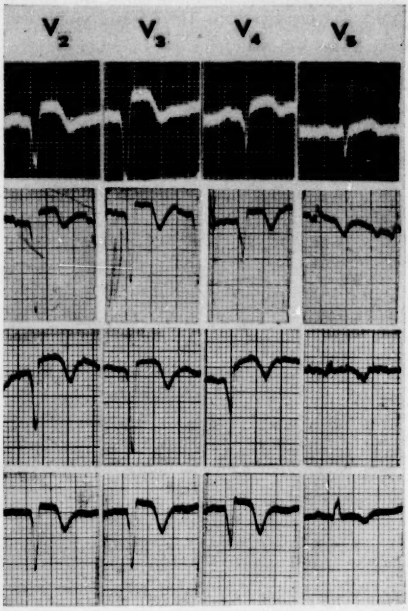

Fig. 4 (case 3).—Fixed acute ECG pattern for eight-year period (ECG's taken, *top to bottom*, Dec. 10, 1948; April 13, 1953; Aug. 22, 1955; and Oct. 13, 1956).

acute anteroseptal myocardial infarction. Despite the observation of a fungating neoplasm of the bladder during cystoscopy, it was decided to postpone the necessary operation for six to eight weeks because of the diagnosis of acute myocardial infarction. The patient's temperature, white blood cell count, and sedimentation rate remained normal. Further questioning revealed a history of acute myocardial infarction two years previously. When the ECG's from the previous hospitalization (fig. 5, *center*) were obtained after 10 days, comparison with the current ECG's revealed a fixed acute ECG pattern (persistence of elevated S-T segments). Cystotomy was performed on April 4, 1957 (an unnecessary delay of two weeks), and a transitional cell carcinoma of the bladder was removed. A follow-up ECG taken four months later (fig. 5, *bottom*) revealed no change from the previous ECG's.

CASE 5.—A 67-year-old man was hospitalized on Sept. 9, 1956, complaining of dyspnea and vague chest pains of six weeks' duration. There was a history of acute myocardial infarction two years previously, treated at another hospital. Physical examination revealed mild congestive failure with bibasal rales and hepatomegaly. There was a visible and

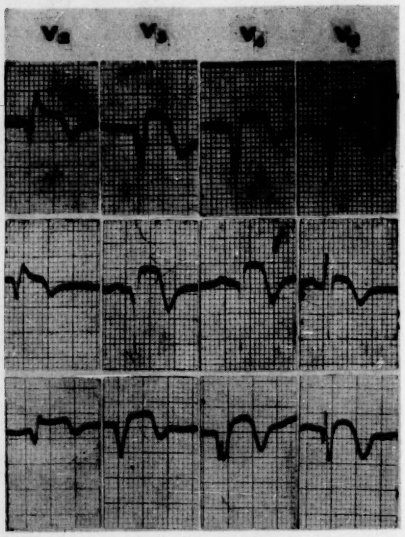

Fig. 5 (case 4).—Fixed acute ECG pattern for four-month period (*top to bottom*, March 20, 1957; June 13, 1955; and July 11, 1957).

palpable precordial impulse in the left fifth intercostal space, medial to the point of maximal impulse. An admission ECG (fig. 6, *top*) was interpreted as indicating an acute anterior wall myocardial infarction. There was no elevation of temperature or increase in sedimentation rate.

Because of the diagnosis of acute myocardial infarction, the patient was kept at bed rest for three weeks. Fluoroscopy on Oct. 3 showed an aneurysmal bulge of the left ventricle, with paradoxical pulsation. An ECG taken on Oct. 23 (fig. 6, *center*) revealed no change from the admission ECG.

At this time the ECG's from the previous hospitalization for acute infarction in 1954 became available. Comparison of ECG's obtained during the current admission in 1956 with those of 1954 (fig. 6, *bottom*) revealed a fixed acute ECG pattern (persistence of elevated S-T segments). It was then realized that the diagnosis of acute infarction made in 1956 was erroneous and that the patient had been hospitalized unnecessarily for six weeks. The discharge diagnosis was aneurysm of the left ventricle.

Comment

After myocardial infarction in some patients, the electrocardiographic pattern of the acute process may persist indefinitely. The ECG pattern of acute myocardial infarction consists of elevated S-T segments, significant Q waves, and inverted T waves in the appropriate leads. Elevation of the S-T segments is considered to be a manifestation of acute myocardial injury and is usually presumptive diagnostic evidence of the recency of an infarction. While the Q waves and inverted T waves may remain as permanent stigmata after an infarction, the elevated S-T segments usually return to the isoelectric line within days or weeks.

In some patients the elevation of the S-T segments associated with the fresh infarction may persist indefinitely (the fixed acute ECG pattern), so that tracings taken months or years later may be misinterpreted as indicating an acute infarction,[1] resulting in diagnostic errors and unnecessarily prolonged hospitalization. The reason for the persist-

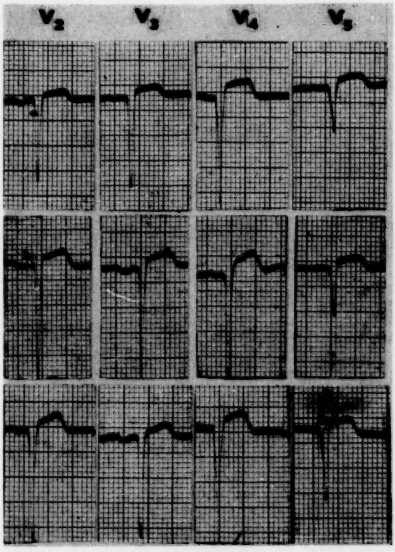

Fig. 6 (case 5).—Fixed acute ECG pattern for two-year period (*top to bottom*, Sept. 9, 1956; Oct. 23, 1956; and Aug. 7, 1954).

ence of the elevation of the S-T segments in some patients is not completely understood. This fixed acute ECG pattern, however, has been noted to occur frequently in patients who develop an aneurysm of the ventricle after myocardial infarction.[2] It is probable that this relationship between ventricular aneurysm and the fixed acute ECG

pattern is not coincidental, since ventricular aneurysm was demonstrated in two of the five cases presented in this paper. One must have a high index of suspicion that, in patients with an atypical history of chest pain and absence of significant clinical or laboratory evidence, electrocardiographic findings suggestive of acute myocardial infarction may represent the fixed acute ECG pattern of an old healed infarction.

Routine serum glutamic oxalacetic transaminase determinations in all cases of suspected myocardial infarction would help eliminate some of these diagnostic pitfalls.[3] The effectiveness of this procedure as a screening measure is limited by the fact that transaminase levels usually return to normal within three days after the onset of an acute infarction. Some of the diagnostic errors in the cases described above might have been avoided by obtaining some detailed histories of possible previous infarction and by the prompt comparison of admission ECG's with tracings taken at other hospitals or during earlier admissions. It should be pointed out, however, that the fixed acute ECG pattern may occur as a result of a "silent infarction" (case 1), so that even a carefully taken history may not be of value.

In patients who have recovered from acute myocardial infarction, follow-up ECG's should be taken at intervals of several months until the pattern has become stabilized. Thus, the presence of a fixed acute ECG pattern can be established and diagnostic errors may be avoided in subsequent emergency situations.

Summary

After acute myocardial infarction in some patients, elevation of the S-T segments may persist indefinitely in subsequent electrocardiograms (the fixed acute ECG pattern). In five patients this fixed acute ECG pattern resulted in erroneous diagnoses of recent infarction years after the acute event, causing needless or unnecessarily prolonged hospitalization. Aneurysm of the left ventricle was demonstrated in two of the five patients; in one the wall of the aneurysm was calcified. Care should be taken to avoid this diagnostic pitfall.

1749 Grand Concourse (Dr. Blinder).

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ACCIDENTAL RADIATION INJURY.—The characteristics of fissionable material vary with the mass and shape of the material. It is said to be "critical" when it is of such configuration that a nuclear reaction can be sustained at a fixed level of intensity. If the critical dimensions are exceeded, an exponentially increasing chain reaction will occur. Accidental excursions of this type produce variable intensities of fast neutrons and gamma rays. Accidents of this nature are referred to as criticality accidents. . . . The general consensus is that when man is exposed to a single whole-body dose of ionizing radiation, he exhibits certain clinical signs, symptoms, and laboratory findings which are collectively termed the radiation syndrome. . . . The radiation syndrome may be thought of as those clinical findings associated with total-body doses of radiation of over 100 rad. The typical . . . sequence of events following a large whole-body radiation exposure can be divided into 4 clinical stages: the initial or prodromal stage, the latent stage, the manifest illness stage, and the recovery stage. The prodromal clinical findings include anorexia, nausea, vomiting, extreme sweating, fatigue, and prostration. These changes remit in the latent period, which begins about 2 days later. After about 2 to 3 weeks of well-being a number of developments begin within a short time of one another. These may include fever, overt or occult infections, scalp hyperesthesia and epilation, purpura and hemorrhage, diarrhea, ileus, cardiovascular collapse, severe lethargy, and changes in sensorium. By about the end of the sixth week after exposure the situation has usually been resolved and clinical improvement of the surviving patients is rapid, although fatigue may continue for some time. . . . About 15% of patients exposed to a dose of 100 rad may be expected to show some of the signs and symptoms of the syndrome. The frequency increases sharply up to the level of approximately 200 rad, at which level most of those exposed would be expected to exhibit some clinical symptomatology.—G. E. Thoma Jr., M.D., and N. Wald, M.D., The Diagnosis and Management of Accidental Radiation Injury, *Journal of Occupational Medicine*, August, 1959.

PULMONARY CHANGES IN HYDANTOIN THERAPY

Matthew T. Moore, M.D., Philadelphia

The roentgenographic characteristics of diffuse fibrosis were observed as abnormal lung findings in a patient who is an epileptic. The x-ray picture remained without change for six years, and there has been no apparent correlation with pulmonary symptoms. Although the patient had no gingival hypertrophy, diagnostic study suggested that the lung tissue changes were due to a drug allergy reaction. The occasionally seen hydantoin hypertrophy of gum tissue is histologically an allergic type of change. Similar lung abnormalities were seen on 16 chest roentgenograms of 31 patients who had taken hydantoin drugs for two or more years. Six of the 15 with normal lungs had gingival hypertrophy as compared to no hypertrophy of the 16 with abnormal lungs. Selective tissue sites of allergic reaction to hydantoin drugs appear deserving of investigation.

The medical literature is replete with reports of the toxic effects of hydantoin derivatives, such as rash, gingival hypertrophy, blood dyscrasia, severe necrosis of the skin, and a wide variety of neurological symptoms which now are readily recognized as a cause-effect relationship.[1] This study deals with a more subtle type of toxic manifestation in the form of pulmonary changes appearing on the x-ray film as accentuated bronchovascular markings, or diffuse interstitial fibrosis, found in patients receiving a hydantoin preparation and which, to my knowledge, has not been reported heretofore. The substance of these observations stems from the data recorded in case 1 below, and the subsequent study of a randomly selected group of epileptic patients who have received a hydantoinate for several years.

Report of a Case

CASE 1.—This patient first came under my care on Oct. 5, 1949, at the age of 42 years. She had been treated for epilepsy since puberty with various anti-epileptic drugs and had received methoin (Mesantoin, methylphenylethylhydantoin) since 1945. The chief complaints on Oct. 5, 1949, were episodic attacks of paroxysmal abdominal pain and a diffuse, measles-like rash involving the extremities and the torso. She had discontinued medication because of the developing rash and subsequently experienced the seizures of abdominal pain. The rash was considered to be due to the methoin, and withdrawal of the drug resulted in complete elimination of the skin eruption, but this was followed by the bouts of abdominal epilepsy.[2] Diphenylhydantoin (Dilantin) sodium was substituted for the methoin, and the attacks of paroxysmal abdominal pain ceased. In a relatively short time she developed an intolerance to diphenylhydantoin in the form of severe ataxia, visual disorder, and speech defect, necessitating a return to therapy with methoin in smaller dosage in combination with a barbiturate, on which she has remained, seizure-free. On April 21, 1953, the patient sustained minor injuries in a taxicab accident, and on May 4, 1953, complained of pain in the left side of the chest, posteriorly. Although no evidence of pulmonary disorder was apparent on physical examination, an x-ray of the chest was obtained. This was reported by Dr. Jacob H. Vastine II, as follows: "There is mottling throughout all of the lung fields suggesting a tracheobronchitis, pneumonitis or possibly an allergy. This is not the usual appearance of tuberculosis, although this patient should be kept under observation and reexamined in 4 weeks." The chest pain disappeared shortly thereafter and, the patient being symptom-free, x-ray studies were not repeated. During the early part of 1954 symptoms of pelvic disorder developed, and on July 26, 1954, a hysterectomy was performed for removal of a large uterine fibroid. The viscera were adherent to the uterine mass, requiring meticulous stripping of the gut from the uterus and adnexa. Convalescence was relatively slow. Pain in the left side of the chest made its appearance again on Sept. 24, 1954, and once more roentgenographic study of the chest was done by Dr. Vastine. The report, in part, read: "Films of the chest show mottled infiltration throughout all of the lung fields. This has not changed appreciably during the past 16 months (fig. 1). The nature of this is not evident. It is probably due to an allergy (Loeffler's pneumonitis). There is nothing which can be interpreted as tuberculosis, neoplasm nor other pulmonary pathology."

It was at this point that the significance of the interpretation of the roentgenographic findings, as possibly due to an allergic phenomenon, occurred to me. I knew of the references in the literature regarding the etiology, pathogenesis, and pathology

From the Graduate School of Medicine, University of Pennsylvania.

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of gingival hyperplasia incident to hydantoin therapy, and that several authors considered the epithelial and collagen hypertrophy to be of allergic origin.[3] Moreover, the patient had normal gums. Why then could not the roentgenographic findings represent proliferation of the epithelial and collagen components of the bronchioles and/or vascular collagen disease similar in nature to that evident in the gums of some patients receiving hydantoin preparations? To test the validity of this concept, 30 additional patients who were on diphenylhydantoin and/or methoin therapy were studied.

A dramatic epilogue to the history of the patient during December, 1958, and January, 1959, highlights the necessity of recognizing the role of hydantoin in producing a form of pulmonary fibrosis, because of the alarm and expense to the patient and the apparently unnecessary array of studies and consultations which were done in hospital. During the latter part of December, 1958, while vacationing in Florida, the patient developed an upper respiratory infection with cough and respiratory distress. The symptoms cleared after two weeks while she was taking an antibiotic. On Jan. 26, 1959, she experienced a mild chill, associated with a cough, and an x-ray of the chest was made at a Miami hospital. She was informed of the scattered opacities in the chest and told they were quite serious. The physician suggested that she return to Philadelphia at once for further study and treatment. She consulted an internist, who admitted her to the Graduate Hospital, University of Pennsylvania, on Jan. 29, 1959. Here extensive hematological studies, heterophil antibody studies, agglutination tests, bacteriological investigations, and roentgenographic studies of the chest and kidneys were carried out. Numerous consultants examined her. During her stay in hospital she was free from pulmonary symptoms. The only finding of significance in the many studies was the scattered mottling of pulmonary fibrosis which corresponded with the films of May 4, 1953, and Sept. 24, 1954. The report of the x-ray department concluded: "In view of the clinical history and previous studies made elsewhere, this may represent some unusual allergic reaction. However, the findings themselves are consistent with sarcoidosis, Loeffler's syndrome, eosinophilic granuloma, or even a granulomatous process such as tuberculosis or fungus. The chest is otherwise negative" (fig. 2). The internist summarized his findings on Jan. 3, 1959, by saying: "There is a remarkable disproportion between symptoms and signs and the extensive pulmonary changes. Tuberculosis, fungal infection, sarcoidosis, lupus erythematosus must all be excluded." After studies were completed he made the final comment: "Without biopsy, I should suggest a diagnosis of suspected

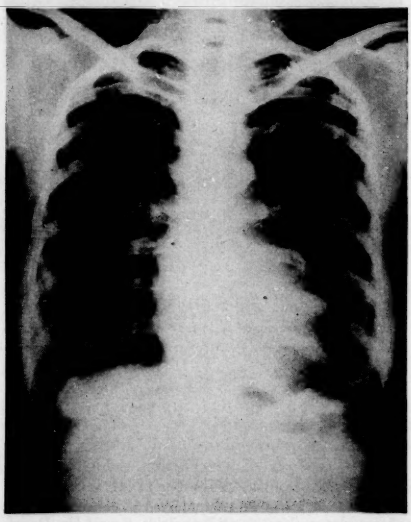

Fig. 1 (case 1).—Sept. 24, 1954. Mottled areas diffusely scattered throughout both lung fields. Identical to film taken May 4, 1953.

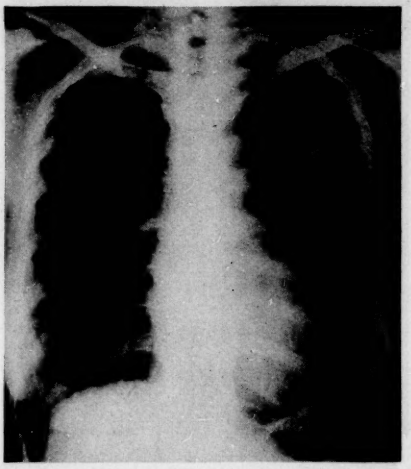

Fig. 2 (case 1).—Jan. 26, 1959. Pulmonary changes are similar to those in figure 1. Gums normal.

pulmonary fibrosis, cause undetermined. Consider patient non-infectious." She was discharged from hospital asymptomatic, and has remained so to date.

Material and Method

Thirty-one patients were selected at random from a larger series of private patients who

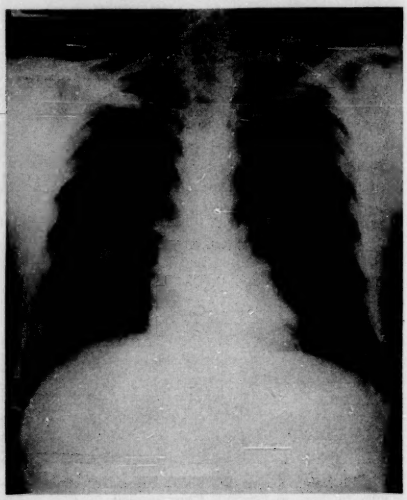

Fig. 3 (case 30).—"Severe accentuation of bronchovascular markings extending into all lung fields." Interpreted as "acute tracheobronchitis." Gums normal.

were receiving a hydantoin preparation, either singly or in combination with a barbiturate, trimethadione (Tridione), primidone (Mysoline), or occasionally amphetamine sulfate. The roentgenographic studies of the chest were done with use of the usual technique. Roentgenographic studies of three patients were done in hospitals, and studies of the remaining 28 were done in a private x-ray laboratory. There were 18 males and 13 females, ranging in age from 13 to 59 years. Twenty-eight of them received diphenylhydantoin sodium, 24 getting diphenylhydantoin only, and 4 a combination of diphenylhydantoin and methoin; 7 patients used methoin, of whom 3 had methoin alone. These patients had received some form of hydantoin continuously prior to this study for periods of from 2 to 12 years. In 27 of these patients there had been no other occasion to perform roentgenographic studies of the chest than for the purpose of this study. The other four cases consisted of case 1, in which the pulmonary fibrosis was a fortuitous finding and diagnosed as stated above; case 22, in which the patient was undergoing extensive study in hospital to determine the cause of convulsive seizures (which proved to be a hemorrhagic cyst of the brain) and in which the chest films were negative; case 26, in which findings on chest films, made in a general hospital, were interpreted as "pulmonary fibrosis"; case 30, in which the patient was an epileptic who had a psychotic episode, and in which chest films made while he was in a psychiatric hospital were interpreted by the roentgenologist on two occasions 19 days apart as "severe accentuation of bronchovascular markings extending into all lung fields—acute tracheobronchitis" (fig. 3). All of the chest films were interpreted by the same roentgenologist on a scale which we rated as follows: 0 = none, + = mild, ++ = moderate, and +++ = severe accentuation of the bronchovascular markings or pulmonary interstitial fibrosis. Similar ratings for the gingival changes were made separately, and the results of both evaluations were tabulated.

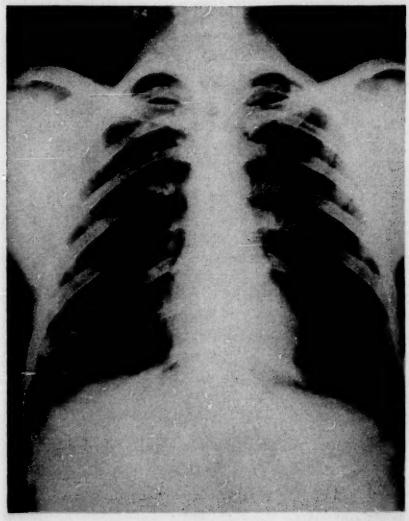

Fig. 4 (case 25).—Oct. 1954. Marked accentuation of bronchovascular markings in all lung fields. Repeat film December, 1955, unchanged. Gums normal.

Pulmonary changes were present, in degrees varying from mild (11 patients) to moderate to severe (16 patients), in a total of 27 patients, or 87%, and gingival hyperplasia was absent (17 patients) or mild (8 patients) in 25 patients, or 80.6%. In the table it will be seen that in those

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patients presenting moderate to severe lung changes (16 cases) gingival hyperplasia was not present at all in 13 and was only mild in 3 instances (fig. 4). Of six patients who exhibited moderate to severe gingival hyperplasia five showed mild lung changes and one showed none (fig. 5, 6, 7, and 8). In only one patient (case 29) was there a combined absence of lung and gingival involvement. Two patients with mild gingival overgrowth showed no lung changes; three patients without gingival changes showed mild pulmonary fibrosis; and three with mild gingival hyperplasia showed a mild counterpart in the lung.

Scale of, and Relation Between, Pulmonary and Gingival Changes in Thirty-one Patients on Hydantoin Therapy

Case No.	Sex	Age, Yr.	Scale of Changes*: Gingival (Hyperplasia)	Scale of Changes*: Pulmonary† (Accented Bronchovascular Markings or Diffuse Pulmonary Fibrosis)
1	F	50	0	+++
2	F	39	+	0
3	F	38	+	++
4	M	41	0	++
5	M	58	0	++
6	M	35	+++	+
7	F	42	0	++
8	F	59	+	+
9	M	46	0	+++
10	F	48	0	+
11	M	13	++	+
12	M	50	++	+
13	M	33	0	++
14	M	18	+	+
15	M	33	0	++
16	F	18	+++	+
17	M	33	0	+++
18	M	35	0	++
19	M	15	+	++
20	F	19	+++	+
21	M	18	+	+
22	F	25	+	0
23	M	38	0	+
24	M	57	0	++
25	M	22	0	+++
26	F	47	+	+++
27	M	31	0	+
28	F	43	0	++
29	F	28	0	0
30	M	36	0	+++
31	F	16	+++	0

* Scale: 0=none; +=mild; ++=moderate; +++=severe.
† Shown roentgenologically.

From the above it would appear that there is an inverse relation between the occurrence of pulmonary fibrosis and gingival hyperplasia. By inference, when the target organ is the lung, the gums escape, and if the latter are involved there is minimal or no pulmonary involvement. Thirteen per cent of the patients had normal lung fields as shown by roentgenographic examination.

Comment

The observation, as seen in the table, of the presence of pulmonary changes in those patients in whom the gum structure is normal, and the reverse in those having gingival overgrowth, can be attributed to more than mere statistical chance. The structural tissue components common to both gums and bronchioles are epithelial cells, collagen fibers, and small blood vessels. Histological examination of both human and experimental animal hydantoin-hypertrophied gum tissue reveals the overgrowth to be due mainly to marked epithelial proliferation and extreme hyperplasia of collagen fibers (fig. 7 and 8). In addition, there is an increase in the size and number of blood vessels

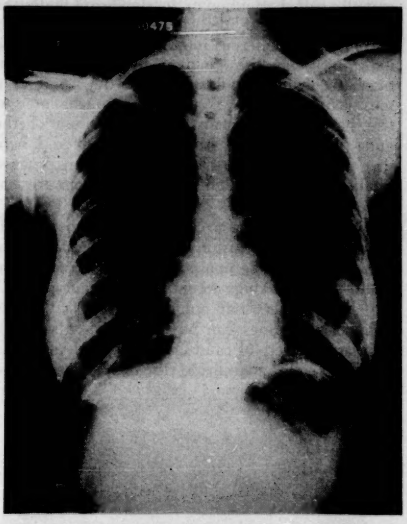

Fig. 5 (case 20).—Minimal prominence of bronchovascular markings in lower lung fields—not in upper. Intense gingival hyperplasia (see figure 6).

Fig. 6 (case 20).—Advanced gingival hydantoin effect.

and lymph channels, as well as varying degrees of inflammatory reaction in the corium.[4] King noted these changes in ferrets given diphenylhydantoin and also called attention to the significant finding of vasodilatation and perivascular proliferation of fibroblasts.[4b] Numerous references have been made indicating that the gingival hyperplasia in patients receiving a hydantoinate is the result of a sensitization process.[3] Since the bronchiolar system has tissue elements similar to those of the gums, it is surmised from the data offered here that the target organ of the sensitization process, in the main, is the lung when the gums are not affected.

When interpreting a chest film, the roentgenologist, lacking the history of a patient, not infrequently renders the nonspecific diagnosis of "bronchovascular markings accentuated beyond normal," or "diffuse interstitial pulmonary fibrosis." These pulmonary findings can be observed as the result of a large variety of causes, among which are some of the so-called man-made diseases [5] secondary to

Fig. 7 (case 31).—Advanced gingival overgrowth. Pronounced epithelial hyperplasia with rete-peg and whorl formation extending well into corium. No pulmonary changes. (Hematoxylin and eosin stain × 100.)

the administration of hexamethonium chloride or hydralazine compounds,[6] drug sensitization resulting in polyarteritis nodosa,[6] and the type of pulmonary changes reported here following hydantoin medication. An inventory of other conditions which may produce the roentgenologic appearance of "pulmonary fibrosis," or diffuse mottled areas of increased "bronchovascular markings" would include histiocytic reticuloendotheliosis [7]; pulmonary hemosiderosis [7]; polycythemia [7]; miliary sarcoidosis [7]; histoplasmosis [8]; coccidiosis; sinobronchitis;

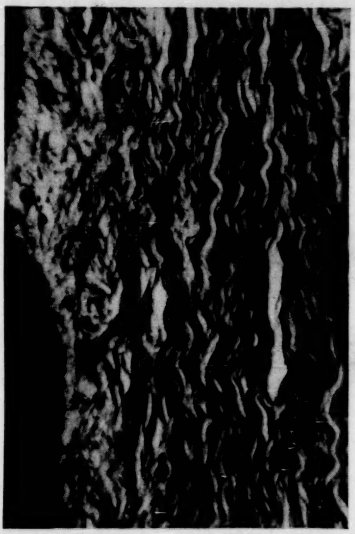

Fig. 8 (case 31).—Extreme hyperplasia of collagen fibers in corium of gum. (Mallory tri-chrome stain × 400).

tracheobronchitis; allergic diseases [7] such as bronchial asthma, hay fever, angioneurotic edema, eczematoid dermatitis; Loeffler's syndrome [9]; collagen diseases such as polyarteritis nodosa, disseminated lupus erythematosus, scleroderma, dermatomyositis; such other skin disorders as erythema multiforme, erythema nodosum [7]; diffuse interstitial fibrosis of the lungs (Hamman-Rich syndrome) [10]; and nickel carbonyl [11] and beryllium poisoning.[12]

Unless the internist and roentgenologist are aware of the relation between the lung findings and the hydantoin effect, they could very well submit diagnoses which would include some of the above and hence be far afield, with the resulting visitation on the patient of dismay, uncalled-for expense, and perhaps erroneous or unnecessary treatment.

Summary and Conclusions

Of a group of 31 epileptic patients on hydantoin therapy, 87% showed pulmonary changes roentgenologically in the form of "accentuated

bronchovascular markings" or "diffuse pulmonary fibrosis." There appears to be an inverse relation between these findings and hydantoin gingival hyperplasia. The possible pathogenesis of this form of pulmonary disturbance must be recognized to avoid erroneous diagnosis and treatment.

1813 Delancey Pl.

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Grateful acknowledgment is made to Dr. Jacob H. Vastine II for the roentgenologic interpretations and ratings.

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ACQUIRED HEMOPHILIA B

REPORT OF CASE WITH DIAGNOSTIC LABORATORY FINDINGS

Seymour Gollub, M.D., Houck Bolton, M.D., Edmund Hessert, M.D.
and
Alexander Ulin, M.D., Philadelphia

A 22-year-old man was hospitalized with complaints of dyspnea and hemoptysis and a history of heart disease and coagulation defects. Repeated study of the clotting mechanism showed the outstanding deficits to be those of thromboplastin generation characteristic of hemophilia B. When the patient's cardiac failure and hepatic dysfunction were relieved, the coagulation defect also disappeared. The hemophilia in this case, therefore, was not hereditary but acquired.

The clinical criteria for the establishment of the diagnosis of classic hemophilia include a bleeding tendency dating from infancy, male sex, a family history of similarly affected males, and transmission of the defect by an apparently normal female. Until recently, laboratory findings of a normal one-stage prothrombin time, prolonged whole-blood clotting time, and a normal platelet count completed a "rigorous diagnosis" of hemophilia. However, with advances in knowledge and the establishment of more precise diagnostic laboratory tests, our understanding of the syndrome has advanced beyond this

From the Blood Coagulation Research Laboratory, Hahnemann Hospital and Medical College, Philadelphia, and West Jersey Hospital, Camden, N. J.

simple formulation. The fact that in approximately one-third of the cases no family history of the expected inheritance pattern was obtainable, and the occurrence of bona fide female hemophiliacs,[1] could not be reconciled with the original formulation.

The demonstration by Pavlowsky [2] in 1947 that plasma samples from different patients with hemophilia could mutually correct each other brought further depth to the problem of hemophilia and suggested the existence of different pathological conditions grouped under the clinical syndrome designated by the single term hemophilia. This situation was greatly clarified by the introduction of the thromboplastin generation test of Biggs and Douglas.[3] As a result of this work it was shown that two distinct pathological entities with similar inheritance patterns, each due to the lack of a different specific protein function occurring early in the coagulation process, gave rise to two indistinguishable clinical conditions. The new pathological entity has been well established and is known as hemophilia B,[4] or Christmas disease. At least four related hemophiloid conditions have been reported.[5] The necessity of the hereditary pattern in the diagnosis of hemophilia is undetermined at present. It has been said that true hemophilia occurs sporadically in 25 to 30% of the total cases recorded. This condition is probably due to mutation, so that hemophiliac males or females arise *de novo*.[6]

Stefanini and Dameshek [7] reported studies in a young woman in whom it was possible to demonstrate deficiencies of both prothrombin and antihemophilic globulin but who had no demonstrable hereditary hemostatic defect. He cited other such cases of apparently acquired hemophilia, one showing spontaneous recovery some months after hemorrhagic symptoms and definitive laboratory studies.

It is the purpose of this paper to report a case of apparently acquired hemophilia B associated with long-standing cardiac failure in a young man undergoing evaluation for corrective surgery. With relief of cardiac failure there was apparent spontaneous recovery, evidenced by lack of hemorrhage or unusual bleeding manifestations at definitive cardiac surgery.

Our materials and methods have been detailed elsewhere.[8] In general, laboratory methods of coagulation analysis have been used in accordance with generally accepted descriptions.[9]

Report of a Case

A 22-year-old man was admitted to the thoracic surgical service of the West Jersey Hospital with a history of long-standing rheumatic valvular heart disease, intermittent cardiac failure, and coagulation deficiencies. Medical history revealed no evidence of cardiovascular disease until the age of 12 years, when he was told he had a murmur and an enlarged heart after an episode of pneumonia.

In May, 1955, he was hospitalized because of progressive exertional dyspnea and repeated bouts of hemoptysis. Physical examination at that time revealed a blood pressure of 130/80 mm. Hg and normal pulmonary findings. The apical cardiac thrust was located outside the midclavicular line in the fifth left intercostal space. Aortic systolic and mitral diastolic thrills were readily palpable. Auscultation revealed a diminished aortic second sound and an accentuated mitral first sound, and at the apex a loud mitral opening snap with a rumbling mitral diastolic murmur and a soft mitral systolic murmur. The liver was unremarkable and the spleen was slightly enlarged and nontender. Fluoroscopic examination of the heart demonstrated a straight left border with an enlarged left atrium in conjunction with lung fields suggesting chronic passive congestion and hemosiderosis. The electrocardiogram showed a wandering pacemaker with a rate varying between 50 and 60 beats per minute. At this time cardiac catheterization was deferred on the basis of an abnormal coagulation evaluation which revealed platelets in the range of 80,000 per cubic millimeter, with decreased prothrombin consumption, abnormal clot retraction, and altered thrombin generation. The serum electrolyte and bilirubin levels were within normal limits, as was the result of the pulmonary function study. The patient was instructed to return to hematology clinic for continued study.

In the ensuing two years, while he was employed as an engineer, the patient's condition gradually deteriorated. He experienced several bouts of questionable heart failure for which he was intermittently digitalized. His exertional dypsnea increased, and the frequency and severity of his bouts of hemoptysis became marked. His hematological picture remained essentially unchanged. In February, 1957, and in November, 1957, the patient underwent repeated cardiovascular surveys at our hospital at which times the physical findings, as noted on his previous admission, were present and in most cases aggravated. During this period the patient underwent repeated study by our coagulation research laboratory for definitive diagnosis of his coagulation defect. In March, 1958, the patient was readmitted with severe palpitations, marked shortness of breath, abdominal pain associated with coughing, and frothy hemoptysis. Physical examination at the time revealed an acutely ill young man in obvious congestive heart failure. The cardiac rhythm was absolutely irregular at a rate of 130 beats per minute. There was a grade-2 systolic murmur heard in the aortic area and an aortic diastolic murmur. The liver was palpated 4 finger-

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breadths below the right costal margin. It was hard and nontender. There was a 2+ pitting ankle edema. An electrocardiogram revealed atrial fibrillation and flutter with a ventricular rate of 130 per minute. Roentgenologic examination demonstrated 3+ general cardiac enlargement, with widespread congestive changes throughout both lung fields. Hospital laboratory studies obtained at that time revealed thymol turbidity, 4 units, and cephalin flocculation, 2+. The patient responded well to treatment and on discharge in May, 1958, he was out of heart failure, effectively digitalized, and free of acute symptoms. The liver and spleen were not palpable. There was no dependent edema and the lungs were essentially clear. The abdomen was normal, and the patient gained weight.

At the end of May, 1958, the patient successfully underwent intracardiac catheterization and several days later tolerated thoracic aortography without evidence of bleeding. The clinical diagnosis of major mitral and aortic stenosis and minor aortic insufficiency was substantiated. In June, 1958, the patient underwent definitive surgery, consisting of transventricular aortic valve dilation and mitral commissurotomy through the left atrial appendage. Hemostasis was secured by electrocoagulation. The patient withstood the operative procedure well and was returned to the recovery room in good condition. Blood loss during the operation was minimal and there was no evidence of abnormal coagulation encountered during or after the operative procedure. His postoperative course was uneventful and uncomplicated. Up to the time of writing the patient has been well and asymptomatic.

TABLE 1.—*Results of Coagulation Studies Made Between February, 1957, and January, 1958*

	2/27/57		3/6/57		1/10/58*	
	Control	Patient	Control	Patient	Control	Patient
Platelet count, per cu. mm.		190,000		194,000		160,000
One-stage prothrombin time, %	100	62	100	85	100	65
Recalcified clotting time	4'20"	7'53"	2'	2'23"	2'15"	3'23"
Inhibitors	5'22"	4'46"(neg.)	2'30"	2'56"(neg.)	2'25"	2'42"(neg.)
Prothrombin consumption, %	83	80	...	...	83	70
Factor VII, %	130 enh.†	140 enh.	...	...	130 enh.	0 enh.
Factor V, %	100	91	...	...	100	100
Fibrinogen, mg. %	165	153	284	268		168
Thromboplastin generation, %	100	22	100	32	100	53

* A lysin determination carried out at this time was negative at 24 hr. for both control and patient.
† Enh: enhancement.

Results.—In table 1 may be seen the results of the coagulation studies done over a period of approximately 10 months, February, 1957, to January, 1958, during which the patient was treated repeatedly for heart failure. The initial study in February, 1957, shows the following outstanding features: mild hypoprothrombinemia, moderately severe thromboplastin generation depression, and prolongation of the recalcified plasma clotting time. Results of further laboratory studies done to find precisely the nature of the coagulation defect are shown in table 2, where it may be seen that the defect in thromboplastin generation resides in the patient's serum and is corrected by normal serum but not by serum from a patient with hemophilia B. Also shown in table 2 are the plasma recalcified clotting times when various normal and deficient plasmas were mixed in proportions of 1:1. These indicate that the patient's plasma does not inhibit the coagulation in normal plasma; that the patient's plasma and the plasma of a patient with hemophilia A are mutually corrective; and that the patient's plasma and the plasma of a patient with hemophilia B are not mutually corrective. Further studies on the patient shown in table 1 done in March, 1957, and January, 1958, show some variation in several of the tests. The most outstanding deficits, however, are those of thromboplastin generation in March, 1957, and thromboplastin generation and factor VII in January, 1958. Special studies done in March, 1957, and January, 1958, on the specific deficit in thromboplastin generation were in general consistent with the studies already referred to.

TABLE 2.—*Results of Further Studies to Determine Nature of Coagulation Defect, Made in February, 1957*

	Control	Patient
Thromboplastin generation corrections, %		
Patient, alone	...	22
Hemophilia B sample, alone	10	...
Normal alumina plasma and test serum	100	25-28
Normal serum and test alumina plasma	100	62-58
Test serum, 1:1 with normal serum and normal alumina plasma	100	84
Test serum, 1:1 with hemophilia B serum and normal alumina plasma	...	23
Plasma recalcified clotting times*		
AHG deficient	10'	...
PTC deficient	5'14"	...
Patient	5'4"	...
Patient and AHG deficient	...	3'25"
Patient and PTC deficient	...	4'35"

* AHG = antihemophilic globulin; PTC = plasma thromboplastin component.

Table 3 shows the detailed results of coagulation studies made during a cardiac operative procedure after the patient had been successfully treated for heart failure. It will be noted that four samples were taken: an initial sample before surgery, a sample during surgery, a two-hour postoperative sample, and a 24-hour postoperative sample. Also included are analyses of the three bottles of blood the patient received over a 24-hour period. It will be noted that the results of these studies are essentially normal. Thromboplastin generation values in particular are within normal limits of our laboratory. The prothrombin consumption values of the

initial sample may perhaps be said to be the only abnormal finding. However, we have not found this test to correlate well with the thromboplastin generation test in our hands.

Comment

Data have been presented indicating the existence of a coagulation defect, identical in results of laboratory tests to the defect known as hemophilia B, in a young man who had no family or personal history of a bleeding tendency. The severity of the defect was somewhat variable over the course of 10 months, but it was definitely present. The alleviation of the state of chronic cardiac failure prior to definitive surgery seems correlated with the disappearance of the coagulation abnormality. Lack of unusual bleeding tendency during and after thoracotomy further emphasized the patient's intact hemostatic mechanism at the time of surgery. The period of time prior to surgery in which laboratory studies were done extended back almost 15 months. From the laboratory point of view there can be little doubt that this patient's defect was identical to that seen in hemophilia B. Indeed, studies done in another institution on this patient were compatible with a diagnosis of hemophilia as long as two years prior to cardiac surgery. It is not our intention to enter into a discussion of the propriety of the particular type of nomenclature to be used in this case. However, it seems clear that the patient in this study shows clinical and laboratory evidence of an impairment in thromboplastin development, due to a functional deficiency of the factor lacking in the condition known as hemophilia B. Further, clinical and laboratory evidence suggest the disappearance of this defect to be associated, in time at least, with the alleviation of the state of chronic cardiac failure and hepatic dysfunction. It is tempting to speculate that the coagulation defect was related to hepatic dysfunction due to chronic cardiac failure.

Table 3.—*Results of Subsequent Coagulation Studies**

	Control	Before Surgery	During Surgery	2 Hr. Postoperative	24 Hr. Postoperative	1st Citrate Bottle	2nd Citrate Bottle	3rd Citrate Bottle
Platelets		160,000	148,000	190,000	190,000	180,000	310,000	140,000
One-stage prothrombin time, %	100	68	90	100	100	85	100	83
Recalcified clotting time	3'27"	3'10"	1'41"	1'57"	2'53"	3'12"	2'2"	2'37"
Inhibitors	2'45"	2'42"	1'52"	1'45"	2'5"	2'37"	1'50"	1'57"
Prothrombin consumption, %	100	66	...	...	...	...	...	...
Factor VII, %	100	56 enh.†	...	240 enh.	105 enh.	...	...	...
Factor V, %	100	...	...	...	...	...	...	...
Fibrinogen, mg. %	320	188	200	215	275	165	220	145
Thromboplastin generation, %	100	87	95	96	86	89	84	72

* Lysin determinations (24-hr.) were negative throughout.
† Enh: enhancement.

Summary

An acquired state of impaired coagulation, with diagnostic laboratory findings identical with those of hemophilia B, occurred in a patient without family or personal history of hemorrhagic or bleeding tendency. Concomitant with the alleviation of chronic cardiac failure and hepatic dysfunction the patient's coagulation studies showed a return to normal, and lack of clinical evidence of impaired coagulation was shown by minimal bleeding encountered during and after definitive thoracic surgery.

230 N. Broad St. (Dr. Gollub).

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CLINICAL NOTES

ASYMPTOMATIC TUBERCULOUS ENTERITIS SIMULATING CARCINOMA OF THE CECUM

Hubert U. Waggener, M.D., James P. Muldoon, M.D.
and
J. Richard Heaton, M.D., Grand Rapids, Mich.

The ileocecal region is the most common site affected in patients with tuberculous enteritis. The roentgenographic studies may show resemblances to carcinoma. The disease is generally seen in patients with advanced cases of pulmonary tuberculosis, and symptoms are ordinarily present. Tuberculosis limited to the intestine is usually of the bovine type. It is rare to see a patient with active pulmonary tuberculosis and extensive tuberculosis of the ileocecal region without symptoms and suggestive physical findings. The following case report is of tuberculous enteritis in a healthy-appearing adult male with a minimal anorectal complaint.

Report of a Case

A 38-year-old man entered the hospital on April 1, 1959, with a chief complaint of an annoying discharge from "near the rectum" of three months' duration. There were no other complaints. Elaboration of the present illness and an extensive review of the systems yielded no additional symptoms. He had been working 8 to 10 hours per day for the past six years. A "spot on the right lung" had been present for 12 years. Periodic chest roentgenograms had showed no change through 1957, according to the patient. He denied any family history of tuberculosis. On physical examination the patient appeared to be a well-developed and well-nourished man in no distress. The only abnormal finding was confined to the anus. Adjacent to the left posterior quadrant was a 2.5-cm. linear ulceration with overhanging edges. Anoscopic and sigmoidoscopic examinations showed negative results.

Results of all blood and urine studies were normal. Roentgenographic examinations of the colon with use of barium enema revealed a persistent, large filling defect of the middle of the ascending colon, strongly suggesting a primary colonic neoplasm (fig. 1) A roentgenogram of the chest (fig. 2) was originally interpreted by the radiologist as showing fibrocalcific deposits in the upper lung fields secondary to a previous tuberculous process but without evidence of activity.

From the Ferguson-Droste-Ferguson Clinic.

An operation was performed on April 6, 1959, with a preoperative diagnosis of adenocarcinoma of the ascending colon. A large, firm, irregular, and constricting lesion of the ileocecal region was found. Multiple loops of distal ileum adhered to this area and were segmentally involved by direct extension of the lesion. Small, narrow, and nodular lesions encircled the ileum in five separate areas. There were large lymph nodes throughout the mesentery. The liver was normal. Gross appearance of the lesion suggested an adenocarcinoma. An extended right hemicolectomy with removal of 60 cm. of the involved terminal ileum was done. Intestinal continuity was restored by an end-to-end ileotransverse colostomy. A biopsy of the anal lesion was done.

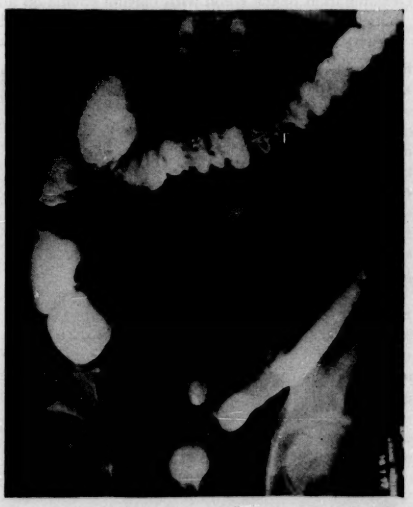

Fig. 1.—Roentgenographic study of colon, showing filling defect in ascending colon.

The opened gross specimen had the appearance of a granulomatous disease rather than carcinoma. Microscopic sections (fig. 3) showed the lesion of the ileocecal region to be composed of multiple tuberculoid areas with groups of Langhans'-type giant cells. Some of the larger lesions contained areas of caseous necrosis. The anal ulcer revealed a chronic nonspecific inflammatory reaction. Special stains of the intestinal lesion showed rare acid-fast organisms suggestive of tubercle bacilli. Tubercle bacilli were identified on direct smear and culture of the sputum and gastric contents postoperatively.

When this was known the chest roentgenogram was reinterpreted as showing probable active pulmonary tuberculosis. Confronted with the diagnosis, the patient admitted that his mother and a sister had died of pulmonary tuberculosis. He had withheld this information because of the stigma he associated with the disease. After an uneventful recovery he was started on medical therapy and transferred to an appropriate facility.

Comment

It is our practice to obtain roentgenographic examination of the colon with barium enema on all patients admitted to the hospital for anorectal surgery. Benjamin and Todd [1] recently reported a

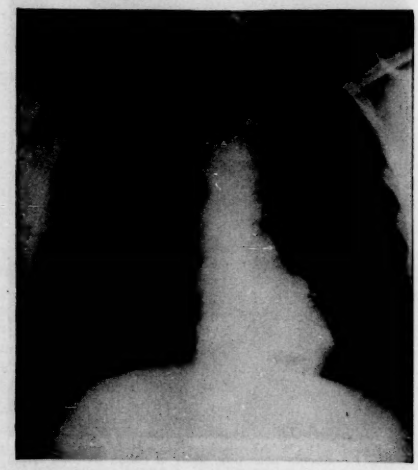

Fig. 2.—Roentgenogram of chest, originally interpreted as showing inactive pulmonary tuberculosis.

series of 8,420 patients, from this clinic, in which x-ray studies of the colon with use of barium enema were done, after careful examination had failed to provide grounds for a diagnosis of colonic disease. Twelve per cent had disease of the colon which had been unsuspected previously. There were no cases of tuberculous enteritis in their series. Our own case is most unusual in that far-advanced tuberculosis of the intestine was discovered in an apparently well patient.

It is reasonable to assume that this patient was certainly approaching the development of symptoms, both pulmonary and abdominal. When seen

Fig. 3.—Microscopic section of intestinal lesion, showing typical tuberculoid areas with giant cell reaction.

for the first time he was still asymptomatic, except for a skin ulcer near the anus. The original interpretation of the one chest roentgenogram was somewhat misleading. A reliable family history would have resulted in more suspicion and a more intensive preoperative evaluation of the pulmonary system. The diagnosis of active pulmonary tuberculosis may have been established. Roentgenographic study of the colon was, nonetheless, strongly suggestive of a neoplasm, and surgical exploration would have been undertaken regardless. The appearance of the lesion at operation was that of an adenocarcinoma, and a resection was performed. The treatment of tuberculous enteritis, when the diagnosis is without question, is medical.

Summary

A case of tuberculous enteritis showed the value of routine roentgenographic examination of the colon in patients with anorectal disease. Tuberculosis of the ileocecal region secondary to active pulmonary disease, without gastrointestinal and pulmonary symptoms, is rare and may easily be mistaken for a neoplasm. When roentgenographic studies suggest malignant disease, surgical exploration is mandatory. The surgical therapy must then be guided by the gross appearance of the lesion and the judgment of the surgeon.

3710 E. Fifth Ave., Denver 6. (Dr. Waggener).

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V. 1

CORNEAL ULCER DUE TO CANDIDA PARAPSILOSIS (C. PARAKRUSEI)

P. Thomas Manchester Jr., M.D.
and
Lucille K. Georg, Ph.D., Atlanta, Ga.

A patient with superficial punctate keratitis, who was receiving antibiotic and steroid therapy, developed an indolent corneal ulcer due to Candida parapsilosis (C. parakrusei). Treatment, which included use of the antifungal antibiotics nystatin (Mycostatin) and amphotericin B (Fungizone), was followed by slow healing of the ulcer.

Report of a Case

The patient was first seen on Oct. 26, 1956, at the age of 37 years. She gave a history of five-year chronic recurrent inflammation of first one eye and then the other. Examination revealed a superficial punctate keratitis of the left eye. The vision was 20/20 in the right eye and only 2/200 in the left. The left eye was amblyopic due to esotropia in childhood. A litmus paper test revealed only 5 mm. of paper to be moist in the right side and only 6 mm. on the left after five minutes. The patient was thought to have keratitis sicca, and methylcellulose eye drops were prescribed to be used every two hours. She did not keep her appointments for follow-up examinations.

The patient was not seen again until Jan. 21, 1958, at which time she was found to have a small central corneal ulcer of the right eye which had been present for approximately 24 hours. A drop of 1% atropine solution was instilled and a patch was applied. When she returned the next day, the ulcer seemed worse. Sulfamethizole (Thiosulfil) was prescribed to be used every two hours; drops of 1% atropine solution were to be instilled morning and night. She was also to take 250 mg. of chloramphenicol (Chloromycetin) orally every six hours.

The corneal ulcer showed little improvement during the next five days, but the chloramphenicol dosage was stopped after the fifth day. Methylcellulose was instilled in both eyes every two hours. In addition, she was given therapeutic doses of vitamin A and vitamin B complex. On March 2, 1958, the eye became painful and an early trace of hypopyon was visible below. The patient refused hospital admission. Routine aerobic and anaerobic cultures revealed no growth of bacteria. Therapy with chloramphenicol was started again, 250 mg. four times daily. In addition, local treatment consisted of drops of tetracycline (Achromycin) solution every two hours and atropine three times a day. The treatment was continued for seven days with no improvement of the ulcer; on the contrary, the hypopyon had increased.

For several weeks the ulcer remained extremely indolent and essentially painless. The eye was not markedly inflamed, although there was a faint aqueous flare several weeks before the hypopyon developed. The ulcer, when stained with fluorescin, had a brownish color, but there was never a marked clouding of the cornea. The center of the ulcer was actually slightly raised and the general appearance suggested keratomalacia. It was approximately 3 mm. in diameter and extended downward only to the outer third of the corneal stroma. At this time a fungus infection was suspected.

Laboratory tests were made at the mycology unit of the Communicable Disease Center to determine whether the ulcer might be due to a fungus. The ulcer was rubbed with a sterile bacteriological loop and material was obtained for direct examination and culture. Wet preparations and stained smears revealed no bacterial or fungal elements. Cultures on Sabouraud dextrose agar with and without antibiotics (chloramphenicol, 0.05 mg. per milliliter, and cycloheximide, 0.5 mg. per milliliter) as well as brain-heart infusion agar were incubated at 25 C, and a similar set of cultures were incubated at 37 C. No growth was apparent for the first 10 days of incubation; however, after this time small white colonies were noted on the plain Sabouraud dextrose agar incubated at 25 C. Direct examination revealed them to be composed of small yeast-like cells. Their slow development and the small number of colonies made it difficult to determine whether this yeast-like organism could be the etiological agent or whether it represented a chance contaminant. Studies were undertaken to determine its identity.

The patient now agreed to hospital admission. Her physical examination showed nothing remarkable. Findings of routine blood studies and urinalysis were normal. Fasting blood vitamin A level was 130 mg. per 100 ml. She was taken to the operating room and the lacrimal puncta were severed and cauterized because of the bilateral tendency to keratitis sicca. A thorough débridement was per-

From the Department of Ophthalmology, Emory University School of Medicine; the Grady Clay Eye Clinic, Grady Memorial Hospital; Atlanta; and the Communicable Disease Center, Public Health Service, U. S. Department of Health, Education, and Welfare.

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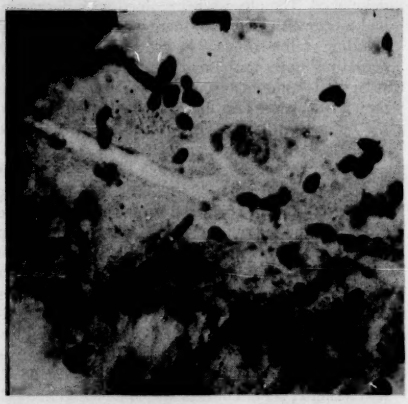
formed on the ulcer, and the corneal scrapings were used for smears and cultures. At this time the everted right upper tarsus had a white, frosted appearance. This area was also scraped for smears and cultures. Gram-stained smears now revealed large numbers of yeast-like budding cells. Some of the buds appeared elongate, suggesting the beginnings of mycelian formations (see figure). Yeast-like colonies developed within a few days on tubes of Sabouraud dextrose agar incubated at room temperature. These cultures, as well as the first obtained, were identified as Candida parapsilosis.

After it had been established that a fungus was the probable etiological agent, use of antibacterial antibiotics was stopped. Administration of atropine and methylcellulose was continued locally, and the patient was given orally 250 mg. of nystatin four times daily and six tablets daily of potassium



Gram-stained smear from corneal ulcer, showing budding cells and beginnings of mycelian formations.

iodine (Iodo-Niacin). In addition, a solution of amphotericin B was given in the form of eye drops, 1 mg. per milliliter every two hours. These drops seemed to burn and hurt the eye and their use was stopped after five days. During the first week of antifungal treatment the ulcer showed very little improvement.

Cultures of the right eye on May 1, 1958, yielded a mixed growth of bacterial and yeast-like colonies. The eye at this time had become slightly more inflamed, and drops of 10% sulfacetamide (Sulamyd) solution were started four times daily. The bacterial culture was identified as Klebsiella species and the yeast-like culture as C. parapsilosis. On May 24, 1958, cultures revealed no growth of either bacteria or fungi, and it was noted that the eye was definitely better. Therefore use of sulfacetamide was continued locally. Drops of nystatin solution were also applied to the eye three times daily. Systemic administration of nystatin was continued for one month after the culture reports were negative. This medication did not cause the patient any pain. The ulcer was definitely smaller on May 31, 1958; and on June 18, 1958, the eye was white and did not stain with fluorescin. The vision still measured 2/200 because there was a deep corneal scar directly over the pupil. The patient was observed six months later and the lesion of the cornea had disappeared except for a thin scar, the eye appearing otherwise normal. The vision was now 20/50 in this eye.

Laboratory Identification of Candida Parapsilosis.—The organism was identified on the basis of its morphology on corn meal agar, its biochemical properties, and serologic reactions.

On corn meal agar cut plates the organism produced abundant mycelium and blastospores. The blastospores were single or in short chains. They were produced at the septa or distal ends of the mycelial cells. Both fine and coarse (giant form) mycelium were observed. The following sugars were fermented: dextrose with acid and gas and sucrose with acid only. Maltose and lactose were not fermented. Sugar assimilation tests showed positive utilization of dextrose, galactose, maltose, and sucrose. Lactose and raffinose were not utilized. Serologic identification was performed with use of monospecific antiserums homologous to antigens of the Candida species. Specific agglutination was obtained with those thermostable antigens which are unique to C. parapsilosis and C. pulcherrima. The latter species was eliminated as a possibility because of differences in morphology and biochemical reactions from the test organism.

Comment

Recent reports [1] have indicated that mycotic infections of the cornea are no longer rare, and there is considerable evidence that the use of antibiotics and steroids in the local management of acute ocular inflammation predisposes to invasion by fungi.

Experimental evidence that local use of cortisone and antibiotics facilitates fungus infections of the cornea has been provided by Ley.[2] This author demonstrated that cortisone, when applied to traumatized rabbit cornea in the presence of potentially pathogenic fungi, resulted in an 80% average incidence of infection, as contrasted with a 20% average incidence in the controls. The broad-spectrum antibiotic oxytetracycline, when combined with the inoculum, potentiated C. albicans infection of the immature rabbit's cornea.

Fungi which have been reported as causative agents in mycotic keratitis include both higher fungi and actinomycetes. Mikami and Stemmer-

man [1a] compiled a list from the literature comprising at least 13 genera. Some of these are fungi which are commonly thought of as pathogenic, such as Aspergillus fumigatus and C. albicans, but the large majority of reports concern fungi usually considered to be saprophytes.

It is important to point out, however, that the isolation of a fungus without demonstration of fungal elements in the tissues does not establish its causal relationship to the disease. In a number of recent reports, however, these criteria have been well satisfied. In other cases, although cultures have not been obtained, fungi have been clearly demonstrated in smears or stained tissue sections from diseased eyes. The table lists the cases of mycotic keratitis which have been proved on the basis of demonstration of fungi in the tissue, with or without cultural isolation of a fungous agent.

The factors which led to the infection in the case described are not known; however, it is known that the patient had been administering self-treatment for a period of two years for recurring episodes of eye inflammation, and it is believed that she used antibiotic and steroid eye drops for this purpose. When the ulcer appeared and the patient returned for treatment, antibiotics were used before its fungous etiology was suspected. There appears to be little question that the ulcer became steadily worse under this therapy. After the finding of yeast-like cells in smears the immediate withdrawal of these drugs and treatment with antifungal antibiotics resulted in a slow but steadily developing recovery.

Summary

A case of corneal ulcer was found to be due to Candida parapsilosis (C. parakrusei). It appears important that the clinician consider fungi in every case of hypopyon ulcer. The clinical and laboratory diagnosis of a corneal mycosis is important, for it demands immediate withdrawal of antibacterial antibiotics and corticoid preparations and institution of appropriate antifungal therapy.

Addendum

Since writing this paper we have learned of a report of three additional eye infections, two due to C. parapsilosis and one to Blastomyces species, published in the *Chinese Journal of Ophthalmology* (7:101-108, 1957).

Mycotic Infections of the Cornea

Year	Observer	No. of Cases	Fungal Agent Demonstrated in Tissue	Culture Obtained
1929	Wright, R. E.: Brit. J. Ophth. **13**:496, 1929	1	"Indistinct mycelium" reported	Glenospora graphii
1942	Bruce, G. M., and Locatcher-Khorazo, D.: Arch. Ophth. **27**:294, 1942	1	Gram-positive filaments	Nocardia
1944	Benedict, W. L., and Iverson, H. A.: Arch. Ophth. **32**:89, 1944	1	Not demonstrated*	Nocardia asteroides, 8 cultures over 4 yr.
1955	Mitsui and Hanabusa [1b]	1	Yeast-like cells	Candida albicans
		2	Mycelian elements	Aspergillus fumigatus
		1	Mycelian elements	Penicillium
1955	Pautler, E. E., and others: A. M. A. Arch. Ophth. **53**:385, 1955	1	Mycelian elements	Monosporium apiospermum
1956	Ley and Sanders [1c]	3	Mycelian elements	.....
1956	Schardt, W. M., and others: Am. J. Ophth. **42**:303, 1956	1	Not demonstrated*	N. asteroides on repeat cultures
1957	Roberts [1d]	1	Yeast-like cells	C. albicans
1958	Gordon, M. A.: Personal communication	1	Mycelium	Allescheria boydii
1958	Haggerty and Zimmerman [1e]	14	Mycelian elements	.....
		2	Yeast-like cells	.....
1958	Mikami and Stemmerman [1a]	1	Mycelian elements	Fusarium oxysporum
1958	Present case	1	Yeast-like cells	C. parapsilosis

*Although fungal elements were not demonstrated in the tissues, these cases were included because a pathogenic fungus was repeatedly isolated from the lesions.

Dr. Takeshi Tsuchiya, of the Department of Bacteriology, School of Medicine, Juntendo University, Tokyo, Japan, performed the serologic identification tests.

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NUTMEG POISONING

Robert C. Green Jr., M.D., Winchester, Va.

The present-day use of nutmeg (Myristica fragrans) is confined largely to exploitation of its properties as a flavoring agent. In the past it has been used medicinally as an aromatic stimulant, a carminative, and a narcotic. In England and India it has been used widely by the laity as an emmenagogue and an abortifacient, and from these uses came many reports of nutmeg poisoning in the early literature. During the last 50 years nutmeg poisoning has seldom been reported, and only limited information is available concerning the physiological and biochemical effects of this particular toxic state.

Review of the Literature

One of the earliest cases of nutmeg poisoning was recorded by de Lobel in 1576.[1] In 1832 Purkinje [2] dramatically illustrated the toxic effect of this kernel by consuming three nutmegs, producing a narcosis which progressed to stupor. In 1903 Wallace,[3] in a review of cases of nutmeg poisoning, reported 25 from the world literature. Although one of the patients concerned died,[4] the remaining 24 recovered promptly without residual effects. Since Wallace's review a limited number of cases of nutmeg poisoning have been noted in the literature.[5] These more recent reports are brief; the clinical descriptions are meager and laboratory studies are not included. It is apparent from these reports and those of Wallace that only limited observation of nutmeg poisoning is available. Therefore, it was felt that a detailed report of such a case from my experience would be of interest.

Report of a Case

A 28-year-old woman was admitted to the Community Memorial Hospital in South Hill, Va., in a semistuporous condition. The medical and psychiatric history up to this time had been normal. She had been married nine years and had experienced two uneventful pregnancies. At 10 p. m. on the night before admission to the hospital she had eaten 18.3 Gm. of finely ground nutmeg in an attempt to induce the menses, which had been delayed two days. She had slept soundly without disturbance until 5:30 a. m. the next day. At that time she had been awakened by a burning sensation in the lower part of the abdomen and an overwhelming feeling of impending death. She vomited once. Her legs felt as if they were asleep and she complained of feeling "funny all over." She had then become completely disoriented, with episodes of wild screaming and purposeless thrashing of the arms and legs. Coordination appeared absent. Interspersed with this disorientation were brief moments of lucidity during which she seemed to be aware of her surroundings. From the time of her awakening at 5:30 a. m. until 9:30 a. m., when she was seen by her local physician, there were three intervals of lucidity, each lasting about 10 minutes. The rest of this time she was delirious and in a state of excitement and agitation.

This patient was admitted to the hospital at 11:30 a. m., about 13 hours after she had taken the nutmeg. On admission she was in a semistupor. She could be aroused to talk, but would immediately return to the semistuporous condition. The skin was cool but not clammy. There was no cyanosis. Blood pressure initially was 100/50 mm. Hg, pulse rate 100 and respirations 24 per minute, and temperature 98 F (36.7 C). The pupils were small and reaction to light was not visible. The thorax was clear to auscultation, palpation, and percussion. The heart was not enlarged and there were no murmurs. The abdomen was not tender and the liver, spleen, and kidneys were not palpable. The extremity reflexes were absent. Pelvic examination revealed evidence of beginning menstrual flow. Results of rectal examination were negative. The erythrocyte count was 3,710,000 per cubic millimeter, and the hemoglobin value was 6.8 Gm. per 100 cc. The leukocyte count was 7,400 per cubic millimeter, with 87% segmented neutrophils and 13% lymphocytes. Results of serologic tests were negative. Specific gravity of the urine was 1.020; the hydrogen-ion concentration was acid. Albumin content of urine was graded 2+; there was neither sugar nor bile. The carbon dioxide–combining power was 14.9 mEq. per liter of plasma. The serum sodium content was 126 mEq. per liter and plasma chloride content, 108 mEq. per liter. The serum potassium concentration was 3.8 mEq. per liter. The value for serum nonprotein nitrogen was 47 mg. per 100 cc.

The patient remained in a semistupor for 12 hours after her admission. She then began to experience episodes of wild excitement, with loud screaming and manifestations of a fear of impending death. She continued to be subjected to episodes of excitement for two hours, during which time restraints were needed. For the remainder of the second day she was restless but essentially quiet. During the third and fourth days of hospitalization she slept much but complained constantly, while awake, of a generalized feeling of numbness and dizziness.

Laboratory investigation on the third day revealed the value for serum nonprotein nitrogen to be 36.5 mg. per 100 cc. The specific gravity of the

From the Medical Service, Community Memorial Hospital, South Hill, Va.

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urine was 1.020; the hydrogen-ion concentration was acid. There was no albumin, sugar, or bile in the urine. The result of the sulfobromophthalein tolerance test was 10.5% retention of dye in 30 minutes. The direct serum bilirubin content was 0.05 mg. per 100 cc.; total bilirubin was 0.35 mg. per 100 cc. The reaction of the cephalin flocculation test was graded negative. On the fourth day of hospitalization the result of a phenolsulfonphthalein test was recorded as 77% excretion of the dye in two hours. Urine obtained during this test had a specific gravity of 1.002; there was no sugar, albumin, or bile. Total serum proteins amounted to 6.1 Gm. per 100 cc., with 4.5 Gm. of albumin and 1.6 Gm. of globulin. The prothrombin time was recorded as 100%. A transthoracic procedure to obtain hepatic tissue for biopsy was done at this time. Microscopic sections of the tissue showed no evidence of fatty infiltration or hepatic cell necrosis.

On the fifth hospital day the patient complained of nausea, dizziness, and generalized numbness. At intervals throughout this day she became restless and noisy and frequently expressed a fear of imminent death. These symptoms persisted intermittently with decreasing frequency and intensity through the sixth day. Between these episodes she appeared essentially normal.

She was discharged on the seventh hospital day. Laboratory studies at that time revealed retention of sulfobromophthalein to be 8% in 30 minutes. The specific gravity of the urine was 1.024; there was a trace of albumin, but no sugar or bile. The hydrogen-ion concentration was acid. The direct serum bilirubin content was 0.15 mg. per 100 cc., and the total bilirubin was 0.95 per 100 cc.

The patient returned for follow-up studies 10 days after discharge. At that time the results obtained from a complete blood cell count; urinalysis; cephalin flocculation, sulfobromophthalein, and serum bilirubin tests; and determination of nonprotein nitrogen remained essentially unchanged from those recorded at previous procedures. She reported that she was without symptoms of any kind. Because of the limited information available concerning nutmeg poisoning no specific therapy was given in this case, except for intramuscular injections of promazine hydrochloride during periods of excitement.

Comment

On the basis of the data in this case and in those noted from the literature it is apparent that nutmeg taken in moderate quantities may produce a serious toxic state and possibly death. To obtain a clearer understanding of the problem the pharmacological and chemical features of nutmeg will be discussed, as well as the clinical syndrome resulting from ingestion of the substance in toxic amounts. Because of the almost total absence of interest in this subject in the recent literature all information concerning the properties of nutmeg have come from a limited number of early studies.

Pharmacological Aspects.—Wallace reported that the toxic factor of nutmeg is confined entirely to the volatile oil component. He administered this oil (0.4 grains [24 mg.] per kilogram of body weight) to cats by a stomach tube and produced a striking clinical response. Within 10 minutes he noted restlessness, excitement, and excessive salivation. These signs were followed by a period of quiet associated with incoordination and staggering. Mydriasis was usually noted at this time. The reflexes became weakened and a condition of semiconsciousness supervened, during which respiration was labored and feeble. In some animals unconsciousness deepened, respiration became labored and feeble, and death occurred 8 to 12 hours after ingestion of the oil. Usually, however, after the stage of unconsciousness had developed, gradual improvement occurred, and about 15 hours after the oil had been given the animal appeared to return to normal. This improvement generally was temporary; the animal then gradually weakened, and within 36 to 72 hours after administration of the oil coma developed and death followed. Autopsy of these animals consistently showed advanced fatty degeneration of the liver.

Dale [6] and Jurss,[7] with use of myristicin, a constituent of the volatile oil, were able to reproduce in animals symptoms identical to those caused by the administration of nutmeg or the volatile oil of nutmeg. They concluded that myristicin is the toxic factor in nutmeg. Autopsy of their animals showed changes in the liver similar to those described by Wallace.

Chemical Aspects.—Nutmeg is known to contain from 5 to 15% volatile oil, 25 to 40% fixed oil, and 5 to 15% ash. The rest is starch, fiber, and water.[8] Power and Solway,[9] in an analysis of this volatile oil, found that 4% was myristicin. The formula for myristicin is $C_{11}H_{12}O_3$, and it is 5-allyl-1-methoxy-2,3,-methylenedioxybenzene. Further analysis of the volatile oil revealed 80% to be dextrocamphene and dextropinene, with 8% dipentene. Also noted were small amounts of eugenol, iso-eugenol, linalool, borneol, terpineol, geraniol, and safrol. In addition, Power and Solway isolated limited amounts of free myristic acid and traces of esters of this and other fatty acids.

Clinical Aspects.—It is apparent from this case and those previously reported that nutmeg in doses of 5 Gm. or more will produce a characteristic clinical syndrome. From one to seven hours after the ingestion of nutmeg symptoms of a burning midabdominal pain, with or without vomiting, may occur. Restlessness, giddiness, and excitement may be noted. Frequently a fear of impending death is reported, and often there is the complaint of a sensation of a heavy weight on the chest. During the next 10 hours drowsiness progressing to stupor

may develop. However, the patient can be aroused; if this is done, delirium and agitation ensue and the patient sinks again into stupor. Some patients may not manifest the early symptoms of toxicity but may display only the late narcotic effect. As a rule recovery is complete within 24 hours. However, large doses of nutmeg may prolong recovery, and periodic outbursts of excitement with delirium may continue for several days or more.

Significant physical findings may include a decrease in blood pressure, with cyanosis and shock. In addition, there may be rapid respiration, tachycardia, dilatation of the pupils, and decreased or absent peripheral reflexes. Several of the early reports suggest that some patients may exhibit, in addition to the usual symptoms and signs, an acute allergic response to nutmeg. This response is manifested by edema of the eyelids, with marked flushing and itching of the face. There also may be an elevation of temperature. These symptoms of an allergic reaction apparently subside quickly.

Some of the laboratory findings in the case I have reported are not entirely understood. Since previous studies did not contain laboratory reports, the chemical determinations recorded in the present case are difficult to evaluate. In this case acidosis was noted, with depression of the values for serum sodium and serum potassium. The serum chloride content was within the normal range.

On the basis of the experimental work on cats by Wallace, Dale, and Jurss it appeared that fatty degeneration of the liver was the end-result of toxic doses of the volatile oil or its derivative myristicin. However, in the case reported here serial studies of hepatic function as well as biopsy of tissue from the liver revealed no evidence of damage to that structure.

Studies of renal function revealed an initial slight elevation of the nonprotein nitrogen value, as well as albumin content of grade 2+, although the output of urine during the first 24 hours was normal. The value for nonprotein nitrogen returned to normal the next day, and a subsequent urinalysis disclosed occasional traces of albumin. It seems probable that in the case presented here nutmeg produced a transient toxic effect on the kidney.

Summary

The toxic factor of nutmeg is known to be myristicin, a constituent of the volatile oil of nutmeg. Nutmeg in doses of 5 Gm. or more produces a marked depressive action on the central nervous system, as well as a less prominent stimulating effect. The clinical course may be severe, with coma, shock, and acidosis as its main features.

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UNDERNUTRITION AND ENDOCRINE DISTURBANCES.—Most patients with this disease [anorexia nervosa] at one time or another are suspected of primary hypofunction of the pituitary or of the adrenal cortex. . . . It is now becoming well recognized that undernutrition itself may lead to multiple endocrine disturbances. Undernourished subjects may show evidence of underfunction of the pituitary, thyroid, gonads and adrenals; Selye cites undernutrition as cause of adrenal exhaustion in his general adaptation syndrome. The whole relationship of the nutritional status to the endocrine system has recently been reviewed by Kennedy and McCance, who point out that multiple endocrine, as well as psychic, disturbances may be mediated through a final common pathway in the hypothalamus. However that may be, hypofunction of any of the endocrine glands does not readily explain . . . body fluid abnormalities . . . [such as] retention of chloride, sodium and water, depletion of potassium and protein, or redistribution of hydrogen.—J. R. Elkinton and E. J. Huth, Body Fluid Abnormalities in Anorexia Nervosa and Undernutrition, *Metabolism: Clinical and Experimental*, July (Part 1), 1959.

SPECIAL ARTICLE

PRIMER ON THE RHEUMATIC DISEASES

PART II

Prepared by a Committee of the American Rheumatism Association

Degenerative Joint Disease (Osteoarthritis)

Degenerative joint disease is a progressive deterioration of diarthrodial joints, characterized by mechanical erosion of articular cartilage and overgrowth of bone at the joint margins. Although this common articular disorder has been variously named osteoarthritis, hypertrophic arthritis, senescent arthritis, arthritis deformans, and arthrosis, the term degenerative joint disease is more accurately descriptive of the pathological changes occurring within the involved joints. The term, however, implies a generalized involvement of the joints of an affected person which is frequently not found. It has had limited acceptance, and the simpler designation, osteoarthritis, is most commonly used.

Etiology.—All of the factors contributing to osteoarthritis are not known. The etiology, however, includes mechanical, dystrophic, and genetic elements. Postmortem studies indicate that the degenerative changes in the cartilage are the earliest anatomic abnormalities and that a correlation exists between the severity of such changes and advancing age, while deterioration of cartilage in the knee joint may be demonstrated in some persons at the end of the second decade of life and is present in 80 to 90% of those over 60 years of age. Furthermore, increased wear and tear through abnormal use of a joint is known to accelerate and enhance the tendency to degenerative changes. Nevertheless, osteoarthritis is typically not a generalized disease but one localized to certain portions of individual joints. This observation, as well as the fact that some persons, even in the latter decades of life, are spared, suggests that the condition is also influenced by processes other than those related to aging and attrition. The exact nature of these other factors, however, remains obscure. A clear-cut relationship between endocrine abnormalities and degenerative joint disease has not been established. Vascular disturbances, arteriosclerosis, and uratic deposits have not been encountered oftener than might be expected in an isolated group of persons of the same age. Focal infection apparently plays no part. Psychic trauma may increase the subjective symptoms but has not been proved to alter the course pathologically.

Articular degenerative phenomena are increased by a variety of functional and anatomic derangements which result in injury to the joint. These include direct trauma, intra-articular fractures, dislocations, penetrating wounds, tears of ligaments or cartilage, osteochondritis, infection, neuromuscular disease, congenital defects, and developmental disturbances. The degenerative joint disease resulting from such conditions is usually spoken of as "secondary osteoarthritis." It is, however, similar to "primary osteoarthritis" except in respect to the time and manner of onset.

Although unproved in other forms of osteoarthritis, a genetic factor seems related to the appearance of the disease in the terminal interphalangeal finger joints (Heberden's nodes). Thus, the incidence of the condition is twice as great in the maternal parent and three times as great in sisters of patients as in the general population. Heberden's nodes, therefore, have a sex-influenced genetic characteristic, dominant in women and recessive in men.

Pathology.—As osteoarthritis progresses, the anatomic changes reflect loss of the inherent ability of cartilage to withstand the abrasive and compressive action incident to normal function. It remains unsettled, however, whether the initial defect occurs in the chondrocytes, in the fibrous proteins, in the unformed elements of the matrix, or elsewhere. Microscopically, a variety of focal degenerative changes have been described in the early phases, including edema and swelling of cartilage cells and chondromucoid softening of the matrix. Subsequently, there is noted mechanical abrasion of the articular cartilage, with tangential flaking parallel to the surface and splitting or fraying perpendicular to it, these latter changes taking place along the lines of collagenous planes. The resultant replacement of the usual smooth, glistening, homogeneous articulating surface by a fine fringed margin is

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The first installment of this primer appeared in the Oct. 31 issue and the third will appear in the Nov. 21 issue.

The Committee of the American Rheumatism Association consists of Drs. Darrell C. Crain, Washington, D. C., Chairman; Wallace Epstein, San Francisco; David Howell, Miami; Harry Margolis, Pittsburgh; Elbert Phelps, Washington, D. C.; William Rawls, New York; Edward Rosenberg, Chicago; J. Edwin Seegmiller, Bethesda, Md.; Lawrence Shulman, Baltimore; Leon Sokoloff, Bethesda, Md.; Harry Thompson, Tucson, Ariz.; and Elam Toone, Richmond, Va.

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spoken of as fibrillation. Local areas of fraying are followed by more extensive disintegration and desquamation, with eventual denudation of the underlying bone.

As this process is taking place within the cartilage, there is concurrent reactive hyperplasia of the adjacent bone. Proliferation of the subchondral connective tissue of the marrow spaces finally involves the subchondral plate in the deeper part of the cartilage. This is thereby invaded, destroyed, and replaced by fibrovascular tissue which becomes ossified to form new bone. Through the constant friction of continued use this reactive bone, which now forms the joint surface in such an area of erosion, becomes highly polished, grossly resembling ivory. It is then spoken of as being eburnated. Comparable processes of reactive bone production occurring at the margin of the articular cartilage give rise to large bony overgrowths, commonly referred to as marginal osteophytes, spurs, or areas of lipping. In the distal interphalangeal joints, however, osteophyte formation has been noted without appreciable concurrent articular damage. Synovitis is usually lacking in osteoarthritis except when minute fragments of joint detritus are displaced into the synovial tissue. Since degenerative joint disease occurs in the older age group a concurrent osteoporosis, either menopausal or senile, may be present, which in weight-bearing joints, particularly the knees, may lead to remolding of epiphysial bone.

Osteophytosis of the spine, often referred to as hypertrophic osteoarthritis of the spine, should probably be distinguished from osteoarthritis of the spinal diarthroses. These osteophytes are formed most commonly at the anterior lateral margins of the ends of vertebral bodies and result from degeneration of intervertebral disks and ossification of the tendon attachments of abnormally stressed muscles. They bear an uncertain correlation to degeneration of apophysial (diarthrodial) joints of the spine. True ankylosis does not occur; nevertheless, varying degrees of spinal rigidity may be brought about by localized osseous bridging at varying points.

Clinical Features.—Degenerative joint disease presents many interesting and puzzling clinical aspects. Although an occasional patient complains of widespread distress, with symptoms in numerous peripheral joints as well as the spine, the majority will localize their complaints to a single joint or at the most to several joints. Furthermore, extensive articular damage may be visible roentgenographically, without significant symptoms. Despite these facts, a fairly uniform clinical pattern can be observed, occurring with increased frequency as persons progress beyond the fourth decade of life. The early symptoms are usually insidious: mild stiffness and aching pain in and about the affected joints, frequently associated with inclement weather. This may persist for many months or years, gradually increasing, with various degrees of severity; in some patients the symptoms remain relatively mild, while other patients become totally disabled. Severe changes occur most commonly in the weight-bearing joints. Physical signs in joints accessible to palpation are minimal soft tissue thickening, crepitus, and changes in the size and shape of the bone as the disease progresses. Effusions are noted only after trauma. In joints not accessible to palpation, such as the hips and spine, the only physical signs are loss of motion and pains on extremes of motion and at times muscle spasm. Constitutional signs incident to the disease are absent; nevertheless, those coincident with advancing years, such as weakness, fatigability, and general senile deterioration, may form an important part of the patient's complaints. In general, pain is more frequent in joints subject to strain, such as the lower part of the spine, hips, and knees, and the severity and nature of discomfort will usually relate to physical activity and the degree of mechanical derangement.

Although any diarthrodial articulation may be involved, some are more susceptible to degenerative changes than others, and symptoms may be influenced by the locality of the involvement. In the hands, the terminal interphalangeal finger joints are most frequently affected. Here, the nodular enlargements at the medial and lateral aspects of the dorsal surface are spoken of as Heberden's nodes. They are more frequent in women than in men, and of concern to the patient chiefly because of the unsightly character of the node rather than because of pain involved. At times, however, an inflammatory period may be present, usually of undetermined cause but at times due to either physical or psychic trauma. Osteoarthritic changes are also seen in the proximal interphalangeal joints and at the carpal-metacarpal articulations of the thumbs. The wrists, elbows, and shoulders rarely have symptomatic involvement and, when present, this is usually associated with occupational stresses or mechanical derangement. A severe form of degenerative joint disease is seen in the hips and is referred to as malum coxae senilis. Inflammatory stages are also recognized in this condition and the progressive nature of the hip involvement makes it a most painful form of the disease and refractory to treatment. Osteoarthritis of the cervical spine is frequently accompanied by degeneration and protrusion of intervertebral disks, at times with radicular symptoms noted in the upper extremities. In the lower part of the spine it is a common cause of persistent backache.

Degenerative joint disease usually pursues a slowly progressive but often intermittent course over many years. While it is not subject to the characteristic exacerbations and remissions of rheu-

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matoid arthritis, periods of improvement, particularly under proper medical management, are frequent, being followed by other periods of symptomatic deterioration or acute episodes related to physical trauma or emotional upset.

Recently it has been postulated that a special form of osteoarthritis can be distinguished from degenerative joint disease and local osteoarthritis. This is spoken of as "primary generalized osteoarthritis" and is characterized by painful episodes affecting multiple joints usually in succession and lasting several months. Inflammatory signs as well as painful symptoms are observed in the distal and proximal interphalangeal joints and in the greater multangular–first metacarpal articulation. Other joints, however, particularly the knees, ankles, and spinal articulations, may be involved. Women are affected 10 times as frequently as men; symptoms are usually worse at night. Despite the fact that symptoms appear in multiple articulations and inflammatory signs may be present, the general health of the patient remains good and there is no sign of systemic disease except for an occasional elevation of the sedimentation rate. Differentiation from rheumatoid arthritis may be difficult. Roentgenography is helpful, since severe osteophytosis is usually seen.

Laboratory and Roentgenologic Observations.—Degenerative joint disease has no characteristic laboratory manifestations. The sedimentation rate may be moderately elevated but is usually normal. Synovial fluid, when present in sufficient quantity for aspiration, has few abnormalities. The total white blood cell count and percentage of polymorphonuclear leukocytes are low.

Roentgenograms reveal narrowing of the joint space, with condensation of bone in the region of the articular cortex and irregular new growths of bone at the articular margins (osteophytes, spurs, and lipping). Discrete subchondral rarefactions (cysts) that sometimes resemble those of gouty arthritis may be present. Bone atrophy of a mild degree is not unusual, but if severe this suggests an associated disease.

Diagnosis.—On clinical examination this disease is not always obvious in the early stages. The presence of articular discomfort in the absence of clear-cut degenerative changes in the joint creates a difficult problem in differential diagnosis. In such instances other causes of skeletal discomfort must be carefully excluded. Intermittently progressive articular aching, relieved by rest and with minimal physical signs of joint disease, in a middle-aged person without evidence of general illness, should lead one to consider the diagnosis. Advanced degenerative joint disease is distinctive, especially when it affects the smaller finger joints, with firm, knobby enlargement leading eventually to deformities and a somewhat limited range of motion. One must be cautious in attributing skeletal symptoms to degenerative changes in the joints, particularly in the spine; and one must avoid misdiagnosis of superimposed disease such as metastatic malignancy, osteoporosis, and intercurrent infections. It is important to remember that the sudden onset of symptoms in previously asymptomatic joints requires an explanation. Degenerative lesions of the spine, especially in the cervical area, may produce symptoms in remote parts of the body.

When the two diseases are present in their classic forms, osteoarthritis and rheumatoid arthritis are dissimilar and should not be confused. Inasmuch as the onset of rheumatoid arthritis not infrequently occurs in later decades, when degenerative changes are common, the two diseases may coexist. If degenerative joint disease involves not only the terminal interphalangeal joints of the fingers (Heberden's nodes) but also the proximal ones, the deformities of the latter may simulate the fusiform swelling of rheumatoid arthritis. The hard, knobby character of the enlargement of degenerative joint disease and the absence of involvement in other joints as the disease progresses is a distinguishing feature. The presence of the "rheumatoid factor" in the serum of patients with rheumatoid arthritis may also be helpful.

Treatment.—Because of the degenerative character of the fundamental disorder, specific therapy does not exist. This form of rheumatism must be managed by the control of symptoms and relief of strains on the affected articulations. Except for degenerative hip or knee disease, which often ends in severe disability, and except for a small number of patients with an apparently marked constitutional predisposition, clinical results with this approach will be gratifying.

General: It is essential to alleviate the patient's fear of becoming helpless by imparting a proper perspective of his fundamentally benign disorder. It is unwise to imply that nothing can be done for him and that he need not return. In some patients coexistent neurotic conflicts and the attendant muscle tension appear to aggravate the disability. Resolution of emotional problems and the attainment of relaxation may produce striking benefits. Food intake should follow a normal pattern, unless caloric restrictions are advisable. Obesity is a common aggravating circumstance, and weight reduction is advisable to relieve abnormal strains on the joints of the lower part of the spine and the legs.

Rest: The most rational therapeutic measures are those combining general rest and individualized care for the affected part. The patient should be instructed to obtain at least eight hours of bed rest at night and, when possible, an additional afternoon rest period. When joints of the lower part of the spine, legs, and feet are involved, additional measures to relieve strain and weight-bearing may

be necessary. Support to various parts can be provided by strapping, belts, braces, or the use of canes or crutches; additional rest in recumbency with or without traction may be required.

Physical Therapy: Physiatric measures are valuable in the treatment of degenerative joint disease and in the correction of improper posture that acts as a contributory factor. During especially painful phases such measures should be confined to applications of heat in a simple form, preferably hot soaks, hot towel packs, or infrared light, accompanied by stroking massage of the periarticular tissues and muscles. After a few days, when the lesion has become quiescent, passive motion should be added before a gradual return to active exercises and normal function. The benefit from roentgenologic therapy for the relief of pain is doubtful, and its use is unjustified when satisfactory relief can be obtained by safer means.

Drugs: Relief from pain and muscle spasm in this disease is usually afforded by therapy with the salicylates, particularly acetylsalicylic acid in doses of 0.6 to 0.9 Gm. three to five times daily. Phenylbutazone is occasionally used, but its administration must be carefully controlled because of its potential toxicity. The simultaneous administration of a mild sedative such as phenobarbital may be helpful in patients with significant nervous tension. Therapy with cortisone and corticotropin relieves symptoms in some patients but is not sufficiently effective to warrant routine use. Intra-articular administration of hydrocortisone in doses of 25 to 50 mg. affords temporary local amelioration of symptoms in most patients and can be a useful adjunct in the management of patients with excessively painful joints. Other glandular elements or vitamins should be given only when a definite deficiency can be demonstrated. Treatment with sex hormones has not proved effective.

Surgery: While the procedures outlined above may ordinarily be relied on to control symptoms and disability from degenerative joint disease, arthroplasty may sometimes be desirable or necessary in patients with badly deformed joints. Such a procedure is aimed at correcting mechanical disturbances and thereby improving motion and controlling pain. Débridement of joints, such as the knee, is occasionally resorted to for removal of hypertrophic bone and smoothing off of articular surfaces. Hip surgery in patients with malum coxae senilis has at times been more successful than surgery on other joints and may be a necessary approach to this particular problem when extensive changes occur. Several procedures are employed; a Vitallium cup over the head of the femur is most frequent, but varying portions of the neck or shaft can be replaced by acrylic or metal prostheses. None is universally satisfactory, and failures occur even when the procedures are performed by experienced surgeons.

Gout

Gout is a familial metabolic disease associated with abnormal amounts of urates in the body and characterized by an early stage of recurring acute monarticular arthritis and a late stage of chronic deforming arthritis, with varying constitutional symptoms. It occurs in all races, nationalities, and social levels. Approximately 95% of patients with gout are men, usually over the age of 30 years; in women the onset is usually after the menopause. From 3 to 5% of all cases of arthritis are probably gouty, although this diagnosis is frequently overlooked. The recognition of gout in one family member frequently leads to establishment of the diagnosis in others. Even more common than overt gout among members of such families is an elevated serum urate level (essential familial hyperuricemia).

Etiology.—The precise nature of the metabolic defect giving rise to the increased blood levels of uric acid in gout is not well understood. The genetic transmission of the trait for hyperuricemia has been attributed to a single dominant gene with incomplete penetrance which is not sex-linked, although recent studies suggest that the hyperuricemia may result from a multiple gene action.

The greatly expanded miscible pool of uric acid found in tophaceous gout demonstrates the dynamic equilibrium of urate deposits with the serum uric acid content. In human beings uric acid arises from two primary sources, the breakdown of dietary purines (the exogenous source) and the catabolism of tissue purines (the endogenous source). Studies of the incorporation of isotopically labeled glycine into uric acid have given evidence in a substantial portion of gouty patients of an excessive endogenous biosynthesis of uric acid direct from its simple and abundant precursors (glycine, CO_2 formyl groups, and the nitrogen of glutamine and aspartic acid), thus bypassing nucleic acid. No specific renal defect in the excretion of uric acid characteristic of gout has yet been demonstrated, although the generally diminished renal function in advanced stages of the disease undoubtedly contributes to urate retention. The precise relationship of hyperuricemia to acute gouty arthritis remains obscure; indeed, it seems possible that some other mechanism unrelated to the blood uric acid level may be responsible, since hyperuricemia not infrequently occurs without acute gouty arthritis.

Pathology.—The characteristic histological lesion of gout is the tophus, a nodular deposit composed of sodium acid urate crystals and the inflammatory foreign-body reaction they have evoked. In the joints, urates are deposited on the surface of the articular cartilage and also in synovial, capsular, and periarticular tissues, including subchondral marrow, periosteum, and tendons. The marrow deposits communicate with the joint space and con-

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stitute the so-called punched-out lesions seen in the roentgenograms. The pathological changes in acute gouty arthritis are not known with certainty, but some recent studies have indicated that urates are present in the synovial tissues in this phase. The chronically affected joint is predisposed to undergo osteoarthritic degeneration, and the joint at times is obliterated by massive tophaceous involvement. Arteriolar nephrosclerosis is commonly found in long-standing cases of gout, while the term gout nephrosis refers to the formation of microtophaceous deposits in the renal pyramids.

Clinical Course.—Individual patients exhibit a wide range of variation in the degree to which their gout is manifest. Some will show throughout life only the features of the disease usually associated with its early stages, consisting of a modest hyperuricemia and infrequently acute episodes of arthritis (acute gouty arthritis). Such attacks, which are self-limiting, subside spontaneously in 4 to 10 days or will respond within 24 to 36 hours to treatment with colchicine and leave no residual effects (intercritical gout). Patients at the other extreme, however, show the full course of the disease, consisting of (1) attacks of acute gouty arthritis recurring at progressively more frequent intervals over the years, (2) markedly elevated serum urate levels, (3) appearance of tophaceous deposits of sodium urate (tophaceous gout) in periarticular and subcutaneous tissues, cartilage, tendon, bone, kidney, and urinary tract, and (4) the eventual progression of the disease through the growth of these tophaceous deposits to a chronic deforming arthritis (chronic tophaceous gout) quite distinct in both pathogenesis and therapy from acute gouty arthritis. In addition, uric acid renal lithiasis occurs in 10 to 20% of gouty patients, and after years of gout renal dysfunction and a tendency to vascular sclerosis may develop.

The acute attacks are provoked by a variety of factors. Among these are such stress-producing events as surgery, trauma, systemic infections, allergens, and emotional disturbances, as well as dietary factors of excessive intake of nitrogenous or fatty foods, ingestion of alcohol, or a weight-reduction diet. Administration of liver extracts, vitamin B-complex, ergotamine tartrate, antibiotics, and mercurial diuretics may also provoke attacks.

Prodromal symptoms may be absent or nonspecific. The onset is characteristically sudden, with complete incapacitation from pain within 12 to 48 hours after the first warning twinge. In a typical case the joint area is warm, red, swollen, exquisitely tender, and excruciatingly painful to move. Bursal effusions, a moderate temperature elevation, leukocytosis, and an increased sedimentation rate may be present. The first metatarsophalangeal joint of the great toe is the first joint to be involved in approximately 25% of cases and will be involved in the early attacks of at least 90% of all cases (so-called podagra). All other large peripheral joints with the exception of the hips and shoulders may be affected. In the early stage the disease is almost always monarticular, but it becomes migratory and polyarticular with recurring attacks.

It is seldom symmetrical. Early untreated attacks usually subside within a week, and the persistence of symptoms more than 14 days in early cases raises a doubt as to the diagnosis. If proper treatment is instituted promptly, symptoms usually subside rapidly; if treatment is delayed, the response is less dramatic and recovery less rapid. Joint recovery is complete and the patient may remain free from symptoms for months or years. Subsequent attacks, however, occur at increasingly frequent intervals and eventually the acute attack will not subside entirely, gradually passing into chronic gouty arthritis associated with tophaceous deposits. This stage of the disease usually follows 10 or more years after the initial gouty attack.

Typical acute gouty arthritis may on occasions accompany blood dyscrasias, such as polycythemia vera, chronic leukemia, myeloid metaplasia, and multiple myeloma, and occasionally constitutes the presenting symptoms. Although referred to as "secondary gout" it is in all clinical respects similar to the "primary" variety, with the exception that a family history of gout is usually lacking.

Laboratory Observations.—An elevation in the serum urate concentration above 6 mg. per 100 ml. in males or 5.5 mg. per 100 ml. in females is found in over 95% of gouty patients and is a useful aid in the clinical diagnosis of gout. A simultaneous determination of blood urea nitrogen level and a complete blood count aid in distinguishing the hyperuricemia of gout from that of renal dysfunction and hematological disorders. In the evaluation of serum urate levels due consideration must be given to the uricosuric action of the antirheumatic drugs, including probenecid (Benemid), ACTH, steroid hormones and phenylbutazone (Butazolidin), and zoxazolamine (Flexin). Although salicylates in doses over 4 or 5 Gm. per day will exert a uricosuric action, they have been found to promote urate retention when given in doses of 3 Gm. per day.

Roentgenologic Examination.—Early in the course of gout, no abnormality can be detected by roentgenographic examination. However, with progression of the disease, tophi are observed as soft tissue swellings around affected joints and as punched-out radiolucent areas of epiphysial bone, particularly in the fingers and toes. In extreme cases this may produce marked erosion and destruction of the bone.

Diagnosis.—The excellent prognosis for most patients with gout, made possible by uricosuric agents, increases the importance of establishing the diagnosis at an early stage in the disease. The possibility

of gout should be considered for any male over the age of 30 years having a first attack of arthritis. The characteristic abrupt onset and other clinical manifestations previously described, coupled with a family history of gout or renal calculi, lend additional support to the presumption of gout. The diagnosis can be confirmed by demonstration of an elevated serum urate level and by obtaining a prompt and complete response of the arthritis to a therapeutic test with colchicine. Acute gouty arthritis is often confused with acute pyogenic arthritis, cellulitis, rheumatic fever, calcific tendinitis, and occasionally rheumatoid arthritis. The diagnosis can be established conclusively in the tophaceous stage of the disease by the demonstration of urate crystals in the contents of a suspected tophus, by either microscopic examination or Weidel's murexide test. Such tophi are found most often about the margin of the ears, in the feet, the hands, and in the olecranon and prepatellar bursae. To establish the diagnosis in difficult cases urate crystals may be demonstrated in synovial tissue obtained at biopsy and fixed in absolute alcohol.

Treatment.—Relief of the presenting acute attack of gouty arthritis should be followed by a carefully individualized program of control to match the severity or stage of the disease.

Acute Gouty Arthritis.—During the acute attack the involved joint should be kept at rest. Local measures for pain relief depend on the patient's preference; use of narcotics may be justified. Once the acute symptoms disappear early ambulation and use of the joint should be encouraged.

Colchicine: Colchicine remains the preferred drug for relief of acute attacks of gout. One 0.5-mg. or 0.6-mg. tablet should be given each hour until either the joint symptoms are relieved or toxicity, manifested by nausea, vomiting, or diarrhea, appears. The diarrhea caused by colchicine often requires treatment with paregoric, 4 ml., or kaolin pectate, 30 ml., given after each loose stool. From 6 to 10 mg. of colchicine is usually required to produce such toxicity, but a therapeutic response is often possible with smaller amounts, especially if the drug is started early in the attack. Patients readily learn to abort many attacks by taking colchicine at the first premonitory symptom. Those who experience more than one or two attacks yearly may be started on therapy with 0.6 mg. of colchicine one to three times daily as a prophylactic regimen for reducing the frequency and severity of attacks.

Attacks can be rapidly terminated by administration of colchicine intravenously in a dose of 2 mg. with a repeat dose of 1 to 2 mg. in six hours, if there has been no response. No more than 5 mg. should be used for treatment of any single attack. Fewer gastrointestinal toxic effects accompany the use of colchicine intravenously, but absence of such warning symptoms could increase the hazard of accidental overdose.

Corticotropin (ACTH): Corticotropin is highly effective in rapidly terminating most acute attacks. It is especially useful in severe attacks and in attacks treated late in their course. A single intramuscular injection of 100 units of long-acting ACTH in repository gel or zinc form will usually result in relief of pain and swelling within several hours. Only rarely is a second injection of ACTH required, but administration of 1.2 to 1.8 mg. daily of colchicine for one to two weeks is necessary to prevent an early recurrence.

Phenylbutazone: Phenylbutazone is an effective agent for producing prompt relief of symptoms of acute gout, usually within 24 hours. It is particularly useful in terminating stubborn cases in which patients have not fully responded to colchicine or ACTH therapy. The initial dose of 400 mg. is given orally, followed by 100 or 200 mg. four times daily for two to three days. After this 1.2 to 1.8 mg. of colchicine is given daily for one to two weeks. Although the potential toxicity of phenylbutazone limits its routine use in gout, complications are rare when its administration is limited to the period indicated. Furthermore, the unpleasant gastrointestinal symptoms which accompany the use of colchicine are not observed. Because of this, many observers prefer phenylbutazone to colchicine in the treatment of acute gouty arthritis.

Steroid Hormones: Although some patients experience improvement from the administration of antirheumatic steroid hormones, the response is less consistent than with other methods of therapy. Their routine use in treating acute gout, or as maintenance therapy, is unwarranted.

Intra-articular Therapy: Hydrocortisone in a dose of 25 to 50 mg. injected intra-articularly into the involved joint is useful in the treatment of acute gout involving a single joint or bursa. Relief of pain is usually prompt and complete within 24 to 36 hours.

Interval and Chronic Tophaceous Gout.—Joint disabilities resulting from tophaceous deposits can be prevented, and to some degree reversed, through the mobilization of urate deposits with prolonged use of a uricosuric agent. Probenecid produces a marked increase in the excretion of uric acid and a drop in the serum urate level. Probenecid should be started at a dose of 0.5 Gm. per day with a fluid intake of at least 3 liters. Alkalinization of the urine to a pH above 6 by administering trisodium citrate, 1 teaspoonful four times per day, may be of help in preventing difficulties from urate calculi, especially during the early stages of treatment. Over a period of weeks the dose of probenecid is gradually increased to that required to maintain the

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serum urate at normal or near-normal levels, usually 1 to 2 Gm. per day. Use of salicylates tends to interfere with the action of probenecid and should be avoided. In the presence of severe renal disease the degree of uricosuria provided by probenecid is often inadequate and more potent drugs are needed to reduce the serum urate level to the normal range. Side-effects of gastrointestinal symptoms or skin eruptions occur in a small proportion of patients receiving probenecid and are an indication for use of a different uricosuric agent. A greater uricosuric action is provided by high doses of sodium salicylates (4 to 6 Gm. per day), but the symptoms of salicylism which frequently accompany this dosage are not well tolerated by most patients. Zoxazolamine and sulfinpyrazone (Anturan) are both highly potent uricosuric agents. Used together they have an additive effect. However, the increased potency carries with it the added hazard of precipitating urate calculi in the urinary tract, especially during the period of initiation of uricosuric therapy. This tendency of uric acid to deposit in the urinary tract can be reduced by a high fluid intake, alkalinization of the urine, and initiation of therapy with low doses of uricosuric agents. An initial dosage of 50 mg. twice daily of either zoxazolamine or sulfinpyrazone should be followed by a gradual increase in dosage over a period of one to two weeks until the desired serum urate levels have been achieved. Maintenance doses in the range of 200 to 400 mg. per day, given in four divided doses, are adequate for most patients. Daily administration of colchicine, 0.6 mg. three times a day, should be given when starting uricosuric therapy in order to suppress the acute attacks of gout that may be precipitated shortly after initiating such therapy. However, with continued uricosuric treatment the frequency of acute attacks is often reduced, and after many months of such therapy tophi may disappear or be arrested and the joint disability may be diminished.

Any one of the following features is indication for institution of therapy with a uricosuric agent in gouty subjects: (1) visual or roentgenologic evidence of tophi, (2) repeated serum urate levels above 8 mg.%, and (3) failure of maintenance therapy with colchicine to reduce the frequency or severity of attacks.

General Measures.—The primary purpose of a low-purine diet is to reduce the amount of uric acid produced by the body from exogenous purines and presented to the kidneys. The extent to which dietary restrictions are needed for control of the serum urate level will be highly individualized, determined by the severity of the manifestations of gout and the response to uricosuric agents.

All patients with gout should be given a well-balanced diet, eliminating such high-purine foods as liver, kidney, brains, sweetbreads, anchovies, sardines, beer, broth, meat soups, and leguminous vegetables. At the beginning of treatment other foods containing appreciable quantities of purines should be eaten sparingly, particularly meat and seafoods. These foods should be limited to 2 oz. (57 Gm.) twice a week, with the remainder of the dietary protein being made up of cheese, eggs, and dairy products. Liberalization of the diet with regard to the latter group of foods may be possible in the patient with tophaceous gout who shows a remarkable response to therapy with uricosuric agents, mobilization of tophi, and a serum urate level in the normal range. In the presence of severe tophaceous gout with marked impairment of renal function the protein content of the diet should be restricted to 50 to 70 Gm., since the endogenous production of purines is directly related to the nitrogen intake. Supplementary vitamins and minerals are of no value in the absence of a specific deficiency. Abundant fluids should be taken habitually to aid in the excretion of uric acid and prevent its precipitation in the urine as stones. The amount of alcohol permitted the gouty patient is a debatable subject. Excessive amounts should always be avoided, and, to be on the safe side, the gouty patient would do well to abstain entirely. In some cases, however, it may be better to permit an occasional drink rather than run the risk of periodic excess. Certain susceptible patients note acute symptoms after the ingestion of very small amounts.

Surgical excision of tophi is seldom indicated. Physical therapy and rehabilitation play as helpful a part in the treatment of gout as they do in the other rheumatic diseases. However, diathermy is seldom well tolerated. Because of the fact that surgery of any type may precipitate an acute attack the gouty patient, when being prepared for operation, should be placed on a purine-free diet for five days before and five days after operation and during that period given colchicine orally, 0.6 mg. three times a day. If an emergency operation is indicated, intravenous administration of colchicine the day of the operation will usually serve to abort an attack.

Collagen Diseases

The term "collagen diseases" is used to indicate several multisystem disorders grouped together because the characteristic pathological processes of each are found widely distributed in the collagenous connective tissues. Involvement of the joints is common. The cause of each disease within the group is unknown; a common etiology or pathogenesis has not been established. Nevertheless, two or more diseases may coexist in the same patient and, at times, symptoms of one may be succeeded by those of another. A common histological abnormality which forms an important characteristic of the group is referred to as "fibrinoid change."

This term refers to the affected tissues, which show a homogeneous, eosinophilic appearance having some of the tinctorial properties of the fibrin. The fibrinoid change may be seen either in the wall of blood vessels or in the connective tissue proper, and the materials responsible for its appearance are deposited in the interstitial matrix substance. Their composition varies, some containing fibrin and others gamma globulin. Systemic lupus erythematosus, polyarteritis nodosa, scleroderma, and dermatomyositis are the diseases usually included in this group. Although the pathological changes described also occur characteristically in patients with rheumatic fever and rheumatoid arthritis, these conditions have been considered separately.

Systemic Lupus Erythematosus

Systemic (disseminated) lupus erythematosus (SLE) is an apparently noninfectious inflammatory disease involving in large part the connective and vascular tissues of many organs and resulting in a variety of clinical manifestations secondary to the multiple system involvement. Although, as the name implies, tegumentary changes were originally regarded as a definitive aspect of the condition, this is no longer the case. The most common symptoms are those referable to the musculoskeletal system, but death ultimately results from visceral involvement. The disease usually runs a chronic course with remissions and exacerbations, periods of relatively good health being abruptly interrupted by explosive episodes. The disease usually begins in the third or fourth decade of life but may start in childhood or old age.

Etiology.—The cause is unknown, Although exposure to sunlight or ultraviolet rays, focal infection, reaction to foreign proteins or drugs, and emotional trauma have on occasions been identified with the onset of the disease or its exacerbations, none is consistently present. The occurrence of several abnormal serum proteins which react with a variety of nuclear fractions to bind complement suggests to many an autoimmune reaction, although such reactions are not definitive proof of their antibody nature. These and other serologic reactions will be discussed in more detail.

Pathology.—At autopsy gross findings are often minimal or absent and even in patients dying with highly active disease few specific histological lesions may be found. In various organs the connective tissue may reveal such nonspecific alterations as fibrinoid change and cellular infiltration, either within the walls of a blood vessel or outside of it. More characteristic changes include "atypical" verrucous endocarditis, disseminated arteritis, thickening of the basement membrane of a glomerular tuft ("wire loop" lesion), and periarterial concentric fibrosis of the spleen. "Hematoxylin bodies" (homogeneous purple masses of altered nuclear material identical with the inclusion body of the L. E. cell) represent the most characteristic histological finding of the disease but are not always present. The renal lesions may vary from focal glomerulitis to diffuse glomerulonephritis. Generalized lymphadenitis with infrequent areas of focal necrosis may be seen. Synovitis when present is of a nonspecific character but will occasionally manifest hematoxylin bodies.

Clinical Features.—Both the clinical picture at onset and the subsequent course are extremely variable. There is little difficulty in recognizing the disease in the patient with classic features of the acute, fulminating disease. These include high fever, symmetrical malar erythema ("butterfly rash"), severe joint and muscle pains, polyserositis, basilar pneumonitis, gallop rhythm, large lymph nodes, nephritis, psychosis or convulsions, and confirmatory laboratory findings. This form of the disease may cause death within a few weeks. In most cases, however, the course is chronic, lasting for years, active periods being interspersed with remissions of varying degree and duration. At the start a single organ system may be involved, with symptoms so vague that it is hard to date their onset. Thereafter, the disease may unfold in an episodic manner over several years. In other cases the onset of the disease may reflect acute involvement of several systems and later become chronic and remitting.

The joints are involved in approximately 90% of patients at one time or another. Arthritis is the initial manifestation in one-third of cases; it is present at onset along with other features in another third. Severe arthralgia, with little evidence of inflammation, is the usual picture, although a migratory polyarthritis involving usually hands, wrists, and knees, resembling rheumatic fever or rheumatoid arthritis, is also seen. Indeed, 30% of patients develop permanent clinically or roentgenologically visible evidence of arthritis, indistinguishable from that of rheumatoid arthritis. Severe deformities and subcutaneous nodules are also noted, but infrequently. Raynaud's phenomenon is not uncommon.

The cutaneous lesions also vary greatly. Most frequently these affect the face, neck, and extremities, especially the fingertips, and may be fleeting or chronic. Included are erythema, follicular plugging, atrophy, purpura, hyperpigmentation or vitiligo, angioneuritic edema, and alopecia. The relationship of discoid lupus erythematosus to the systemic disease is not clear. There are patients with SLE who first had the chronic discoid form for several years; other patients begin with the acute form and subsequently develop discoid lesions.

Half of the patients have local or generalized adenopathy. One-third have hepatomegaly, but jaundice is rare. The spleen is enlarged in only 15 to 20%. Pleurisy with or without effusion is noted

in over half the cases and may be associated with an atelectatic pneumonitis, seen in 20%; a similar proportion have a complicating bacterial pneumonia. The heart is also involved in over one-half of the cases. Pericarditis is common, but large effusions are unusual. Myocarditis may lead to heart failure. Valvular lesions are only rarely associated with functional aberrations. Gastrointestinal symptoms include dysphagia, anorexia, nausea, vomiting, abdominal pain, diarrhea, and melena.

Renal involvement is a common and a serious feature of SLE. It begins as a focal glomerulitis, at which time urinalysis reveals only white blood cells; it may then pass through the nephrotic stage to the terminal picture of subacute glomerulonephritis with uremia and usually hypertension. Many patients exhibit neurotic or psychotic behavior, usually in a paranoid form, and some have convulsions. These reactions usually coincide with highly active disease and are ominous signs. Peripheral neuritis is rare. More than 25% of patients have retinal lesions. The most frequent finding is small white spots in the nerve fiber layer of the retina, called "cytoid bodies."

Laboratory Findings.—Anemia is found in 80% of cases. This is usually moderate and of the normochromic and normocytic variety. Severe hemolytic anemia, probably not due to hypersplenism, is found in 5% of cases. Some patients with SLE show antibodies against red blood cell antigens; but transfusion reactions are not excessive. Purpuric lesions are common. One of several factors is responsible: involvement of small vessels with SLE, azotemia, thrombocytopenia, or in rare instances a peculiar circulating anticoagulant or prothrombin deficiency secondary to liver disease. The white blood cell count is usually low normal or slightly subnormal. Extreme leukopenia is rare.

The erythrocyte sedimentation rate is elevated in almost all patients with active disease and may remain high in clinically apparent remissions. In half the cases there is an increase in the serum globulin concentration, usually in the gamma and alpha-2 fractions, and there are also positive cephalin-cholesterol flocculation and thymol turbidity reactions. Other evidences of plasma protein dysfunction include red blood cell autoagglutination, circulating anticoagulant, positive result of Coombs' test, cryoglobulinemia, lowered serum complement activity, the presence of the rheumatoid factor in up to 34%, and a chronic biological false-positive result of the serologic test for syphilis in 20% of cases.

Another important serologic reaction is the L. E. cell phenomenon which, if present, strengthens the diagnosis, with certain reservations. A typical L. E. cell is a polymorphonuclear leukocyte, largely filled with and enlarged by an inclusion body, a globular mass of homogeneous material appearing like ground glass and staining red-purple with Wright's stain. The same material may be observed extracellularly as free "globs" or "rosettes," i. e., globs surrounded by neutrophils. Three factors are essential for L. E. cell formation: (1) a serum factor, acting on (2) damaged leukocytic nuclei, and (3) phagocytic cells to engulf the altered nuclear material. The test is carried out in vitro and only the serum factor must come from the patient with SLE. It resides in the gamma globulin fraction. The reaction between L. E. factor and nuclear material is complement-fixing.

The incidence of positive L. E. cell test results in patients with SLE is 69 to 100%, but such figures have limited significance, considering the lack of satisfactory criteria for the diagnosis of SLE. There are three interesting "false-positive" categories; the hydralazine syndrome, consisting of rheumatoid symptoms occurring in patients treated over long periods of time with hydralazine; various hepatic disorders; and other "collagen diseases" (in both rheumatoid arthritis and scleroderma the incidence of false-positive test results may approximate 15% or more of all cases). The correlation between the number of L. E. cells observed and the activity of SLE is poor.

Roentgenograms of the chest may reveal disk-like atelectases at the lung bases and cardiomegaly. The degree of renal involvement is reflected in the urinalysis, where albumin, red blood cells, and hyaline or granular casts may be found.

Diagnosis.—The patient with a classic clinical picture, compatible biopsy findings, and a positive L. E. cell test result poses no diagnostic problem. This, however, is not the usual mode of presentation. The disease generally unfolds in an episodic manner, and at the beginning, or even later, only one manifestation may be dominant. In such situations a careful history may disclose previous unexplained illness, or there may be concurrent atypical clinical, physical, or laboratory findings, evidence of protein dysfunction, or a positive L. E. cell test result. Punch biopsy of the kidney may be helpful in cases with renal involvement.

The differentiation between SLE and other rheumatic disorders may be difficult. An example is the "rheumatoid arthritic" who has fever, subcutaneous nodules, pericarditis, anemia, and L. E. cells. To some it would seem that this patient has severe rheumatoid arthritis and a false-positive L. E. cell test result; to others, that he has SLE with prominent joint involvement. This problem has not yet been resolved.

Prognosis.—The outcome may be death in a few weeks or a benign course lasting decades. The death rate after diagnosis is estimated to be constant at 10% per year.

Treatment.—Treatment with steroids may produce dramatic improvement but should be prescribed only for severe acute attacks or for significant involvement of a vital organ system. At such times administration in adequate doses may be lifesaving.

The amount of steroid necessary is usually considerably higher than that used in the control of rheumatoid arthritis. Thirty to forty milligrams of prednisone per day is an average dose, but some patients may require two or even three times this amount. The drug should be withdrawn as the acute exacerbation subsides.

Between attacks, or during exacerbations of modest severity, therapy with salicylates may lessen fever and joint pains. Otherwise, treatment is purely symptomatic. Synthetic antimalarial compounds such as chloroquine sulfate and dihydroxychloroquine phosphate apparently have a beneficial effect on some of the cutaneous lesions but are otherwise of questionable value. Patients should be advised to avoid exposure to the sun and should be cautioned about possible adverse drug reactions.

Polyarteritis (Periarteritis) Nodosa

Polyarteritis nodosa is an apparently noninfectious disease characterized by segmental inflammation of medium-sized or small arteries, with varying multisystem manifestations, depending on the site of arterial involvement. It may appear at any age but is most common in middle life; the incidence is greater in males.

Etiology.—The cause of the condition is unknown. Necrotizing arteritis similar to the human lesion can be produced in experimental animals by sensitization to foreign protein and by other means. Moreover, polyarteritis has been found in some patients dying of serum sickness or of apparent hypersensitivity to such drugs as sulfonamides, arsenicals, iodides, and penicillin. In the majority of cases, however, careful questioning fails to reveal evidence of sensitization. It is possible that a number of etiological agents and diverse pathogenic mechanisms may be involved in the development of the lesion.

Pathology.—Histologically, the active arterial lesions show segmental necrosis, fibrinoid change, and infiltration with leukocytes. Eosinophils may also be present but are not essential for the pathological diagnosis. Attempts at repair may result in complete healing, fibrosis of the adventitia producing the nodules (which may be detected clinically), or intimal proliferation together with thrombosis and infarction. These lesions may affect the entire circumference of a vessel or only a portion. Aneurysmal dilatation of the vessel wall may lead to its rupture. The usual picture at autopsy consists of vessels exhibiting various stages of inflammation and repair. No single set of vessels is found to be involved in every case. Any organ may be affected. Most frequently, however, the lesions are seen in the kidney, peripheral nerves, muscles, gastrointestinal tract, heart, and liver.

Some investigators divide the angiitides into several types, depending on histological features, distribution of lesions, and the associated clinical condition. It remains to be determined whether or not such divisions are justified.

Clinical Features.—Symptoms and signs are so protean that no typical description is possible. The onset may be acute or insidious. The disease may appear as (1) fever of unknown origin; (2) primary renal disease, thought to be glomerulonephritis; (3) severe abdominal pain, often with hematemesis or melena; (4) bronchial asthma or bronchopneumonia; (5) cardiac failure; (6) muscle pains and weight loss; or (7) painful peripheral neuritis, often bilateral.

It is usually a combination of features that suggests the correct diagnosis. Renal involvement is the most frequent. Hypertension is present in more than half the cases. Cutaneous manifestations may include erythematous eruptions, bullae, purpura, and subcutaneous nodules. Nodules have a linear distribution along the course of arteries. Arthralgias, polyneuritis, and myositis are common, but true arthritis is relatively rare.

Laboratory Findings.—Leukocytosis, with a shift to the left, is usually noted, although the white blood cell count may be normal or low. Eosinophilia is particularly apt to be present in patients with bronchial asthma. A mild normocytic anemia is common; severe anemia is usually the result of blood loss. Albuminuria and hematuria are the common urinary abnormalities, although white blood cells and casts may also be seen. The sedimentation rate is usually elevated and the serum globulin level is often elevated.

Diagnosis.—The correct diagnosis may be suggested by the clinical and laboratory findings, but biopsy remains the sole means of establishing it with certainty during life. Even so, only one-quarter to one-third of random biopsies done on patients later proved at autopsy to have the disease have been shown to be positive. Material for biopsy should be obtained from a painful area, if possible, and adequate (2 by 1 by 1 cm.) specimens of muscle are desired. Because of the segmental nature of the involvement serial or multiple sections may be necessary to demonstrate the lesion.

Arteritis similar to that observed in polyarteritis nodosa may also be found in rheumatoid arthritis, systemic lupus erythematosus, scleroderma, and, less frequently, rheumatic fever. The relationship between that found in polyarteritis nodosa and that found in rheumatoid arthritis has been discussed more fully under the latter disease.

"Wegener's granulomatosis" is characterized pathologically by necrotizing granulomatous lesions of the respiratory tract, generalized arteritis, and focal glomerulitis. Clinically, it begins with severe destructive sinusitis or rhinitis or persistent pneumonitis, followed by signs of renal damage and generalized vasculitis.

Prognosis.—The prognosis generally is poor, with death the usual outcome after weeks or months of

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illness. However, patients may live for years, enjoying good health, when vital organs are not severely involved.

Treatment.—No specific therapy is known. Although the number of cases responding favorably to treatment with steroid compounds is discouragingly small, a therapeutic trial is justified. Supportive measures may be of value. Every effort should be made to eliminate any potentially offending antigen.

Scleroderma

Scleroderma is a chronic disease characterized by fibrous thickening of the dermis and the connective tissue of various internal organs. Because viscera are often affected it is at times referred to as "progressive systemic sclerosis." It is not rare. The peak incidence is in persons between the ages of 30 and 50 years, although it may affect persons of any age; it is more frequent in women than men. The course is usually slowly progressive.

Etiology.—The etiology is obscure. There is no evidence to support the concept of hypersensitivity. The autonomic nervous system has been implicated by the frequency of Raynaud's phenomenon and the reported improvement after sympathectomy in some patients. The presence of a psychological component in most cases is of interest.

Pathology.—Early in the disease sections of the skin may appear normal. As the condition progresses the dermis is thickened by coarse collagen bundles lying parallel to the surface of the skin. This fibrous deposit frequently extends into the subjacent adipose tissues. Hyalinization may eventually occur, with loss of all skin appendages. Calcification in the skin is not uncommon. Fibrosis commonly occurs in other organs, including the alimentary tract, myocardium, lung parenchyma, and muscle.

Vascular lesions involving small arteries and arterioles are found in the majority of cases at autopsy. The kidney is the most frequent site. The lesion may be chronic, with marked intimal fibrosis, or it may be acute, with deposition of fibrin-like material beneath the endothelium. The latter may be associated with platelet thrombosis of arterioles and capillaries. Focal glomerular necrosis or cortical infarctions are present in many instances. Glomerulonephritis is not found. Chronic myositis and fibrinous synovitis are also common findings.

Clinical Features.—The onset is characteristically insidious. Stiffness of the fingers and hands may be an early complaint. Raynaud's phenomenon and hyperhidrosis of the palms and soles may antedate other manifestations by months or years. The earliest lesions of the skin are found usually in the hands or feet, less commonly in the face and neck. These consist of a diffuse, nonpitting edema, usually without erythema. The involved skin then becomes waxy, taut, hard, thickened, and finally bound firmly to the underlying structures. Normal skin folds disappear, producing a mask-like appearance in the face. The process may then spread centrally from the distal parts of the extremities and involve the entire integument. Brown pigmentation and vitiligo are common. The fingers may become immobilized in flexion. Ulcers, difficult to treat, appear on the fingertips and at pressure points over joints. Both diffuse subcutaneous calcifications (calcinosis universalis) and periarticular calcifications (calcinosis circumscripta) are seen. Recurrent polyarthritis is common but rarely leads to deformities.

Dysphagia and sour eructations due to esophageal involvement are common and may precede skin involvement. Small-intestinal disease may appear later, with symptoms suggesting obstruction or paralytic ileus.

Pulmonary symptoms, usually tachypnea and dyspnea, may result from sclerodermatous encasement of the thorax impeding respiratory motions or impairment of alveolar diffusion secondary to fibrosis of the lung parenchyma. Aspiration pneumonia may result from difficulty in deglutition. Involvement of the myocardium may cause arrhythmias, conduction defects, and heart failure. Renal involvement, with uremia and malignant hypertension, is a common terminal event.

Laboratory Findings.—Blood studies give normal results except during periods of active disease, at which times the erythrocyte sedimentation rate is elevated and the serum protein content altered, with a reversal of the normal albumin:globulin ratio. When renal involvement supervenes the urinalysis shows albuminuria, red blood cells, and casts. The serum calcium, phosphorus, and alkaline phosphatase activity are normal in the presence or absence of calcinosis. Roentgenograms of the involved parts may reveal osteoporosis, destruction of the distal phalanges, and subcutaneous or periarticular calcifications. The esophagus may be dilated and without normal peristaltic activity. The antrum of the stomach may be constricted and the small intestine segmentally dilated. Roentgenograms of the chest may reveal diffuse pulmonary fibrosis, occasionally with small cysts.

Diagnosis.—Dermal changes are characteristic in the well-developed cases and may be confirmed by biopsy. Early changes in the fingers may simulate those of rheumatoid arthritis or systemic lupus erythematosus. At times patients may appear with simultaneous clinical and laboratory characteristics of scleroderma, as well as rheumatoid arthritis, systemic lupus erythematosus, and dermatomyositis. Progressive systemic sclerosis should not be confused with "morphea," or localized scleroderma, in most cases of which there is no evidence of extracutaneous disease.

Prognosis.—A prolonged, progressive course of many years' duration is the rule. In some cases

death results from renal involvement, with rapidly advancing malignant hypertension, or from pulmonary or cardiac dysfunction.

Treatment.—No specific remedies have proved to be of consistent value in the treatment of the disease. Physical therapeutic measures should be applied to combat contractures and preserve muscle strength. Sympathectomy usually fails to give more than transient relief, principally from the vasomotor phenomena.

Dermatomyositis

Dermatomyositis is an ill-defined disorder characterized primarily by chronic nonsuppurative inflammation of the skin and striated muscles. The term "polymyositis" is used when there is only muscle involvement. It may affect persons of any age; although it is most common in middle life, its incidence in children is appreciable. It is slightly more common in females.

Etiology.—The cause is unknown. However, the incidence of neoplastic disease in dermatomyositis is much greater than would be expected on the basis of chance alone, being reported in as many as 34% of adult cases. The tumors are of various types and from different primary sites. The relationship between the two conditions, however, remains a mystery, since symptoms of dermatomyositis frequently continue after successful therapy of the associated tumor.

Pathology.—Variable nonspecific patterns of dermatitis are seen. The muscles may grossly appear pale, with areas of yellow or pink patches of discoloration. Histological alterations in striated muscle include atrophy, necrosis, hyalinization, and fragmentation of the fibers; proliferation of sarcolemmic nuclei; and occasional scattered giant cells. Lymphocytes, plasma cells, and histiocytes are seen around small blood vessels or in other parts of the muscle. Multiple gastrointestinal ulcers occur with some frequency.

Clinical Features.—The onset may be explosive or insidious, with low-grade fever, weight loss, malaise, weakness, and muscle aching. Raynaud's phenomenon may be present. Edema of the face, particularly striking in the periorbital region, is associated with a purple-red (heliotrope) discoloration. The skin over the face and V-area of the neck may appear diffusely red or telangiectatic. The dermatitis elsewhere is quite variable. Mottled or diffuse erythema, with or without edema and often desquamating, is common on the extensor surfaces of the arms and legs as well as on the trunk. Later in the disease there may be patchy hyperpigmentation or subcutaneous calcification, with extrusion of calcific deposits through the skin.

The most important feature is the muscle involvement, which is manifested by aching, tenderness, weakness, and stiffness. Characteristically, the proximal muscle groups of the upper and lower extremities are more frequently and severely involved than the distal ones. Because of this, the patient may be unable to comb his hair or maintain a steady gait. With more severe involvement he is unable to sit up in bed or lift his head from the pillow. Initially the muscles may feel doughy and later, firm. With further progression they become atrophic and fibrotic, with contractures of shoulders, elbows, hips, and knees. Arthralgia may be an early complaint, but there is little, if any, arthritis.

Involvement of specialized muscles may produce such functional changes as palsies of extraocular muscles with diplopia, dysphagia, hoarseness, or ventilatory insufficiency. Ulcers of the alimentary tract may be encountered in patients with late cases.

Laboratory Findings.—The erythrocyte sedimentation rate is elevated during active periods. Slight anemia is common. The white blood cell count is usually normal, but there may be a transient eosinophilia or monocytosis. The serum globulin concentration may be modestly increased. As in other muscle-destroying diseases the urinary excretion of creatinine is reduced and that of creatine raised. The serum glutamic oxalacetic transaminase (SGO-T) level is usually elevated. The electromyographic changes are nonspecific. Roentgenologic examination may reveal extensive subcutaneous calcifications, which in some cases are concentrated periarticularly.

Diagnosis.—The diagnosis is made largely on the basis of the clinical picture and may be strengthened by compatible muscle or skin biopsy findings. Early in the disease, however, it may be difficult to distinguish dermatomyositis from progressive systemic sclerosis, scleredema, or systemic lupus erythematosus. When the cutaneous manifestations are absent or minimal, such muscle disorders as myasthenia gravis, progressive muscular dystrophy, or thyrotoxic myopathy must be excluded by specific laboratory tests for these disorders.

Prognosis.—Death is the outcome in about half the cases. Although the disease may be rapidly fulminating, the usual course is one of moderate progression. Those surviving the first year have an excellent prognosis for life but may be left with crippling muscular defects.

Treatment.—Therapy is largely symptomatic. Of all the agents tried, only the adrenocortical steroids offer any hope of combating the disorder. In most patients there is no response to therapy with steroids, but the occasional striking improvement warrants a full trial. Physical therapy may help to preserve maximal use of unaffected muscle and prevent contractures. In view of the supposed improvement in some cases after removal of a malignancy, a thorough search for tumor should be carried out.

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COUNCIL ON DRUGS

Report to the Council

The Council has authorized publication of the following report.

H. D. Kautz, M.D., *Secretary.*

CURRENT STATUS OF THE THERAPY OF BURNS

Isidor S. Ravdin, M.D., Philadelphia

Many of the most important aspects of the therapy of burns have not changed to any significant degree in the last few years. The need for supportive therapy of a general character, gentleness in the handling of the patient, and exacting cleanliness in the handling of the burned patient are just as fundamental today as they were before the days of chemotherapy, of transfusion, and of fluid and electrolytes. These fundamental principles apply to the patient as a whole, as well as to the local wound. They, very likely, outweigh recent contributions which have been made in the care of the burned patient.

General Considerations

Significant strides have been made in the treatment of shock with the greater use of blood, plasma, and, at times, plasma expanders. Significant progress has been made in the prevention of electrolyte imbalance, its recognition, and correction. Septicemia, the greatest cause of death in the salvable burned patient, has been curtailed by the judicious use of antibiotics. It is important, however, to point out that the routine prophylactic use of systemically administered antibiotics is probably contraindicated except in the very severe burns. When antibiotics are indicated, they should be changed every few days to minimize the development of resistant strains of organisms. When staphylococcic infection occurs, the strains should be rapidly determined, and the antibiotics used should be those to which these strains are sensitive. The use of cortisone (Cortisone, Cortogen, Cortone) acetate and corticotropin (Acth, Acthar, Corticotropin) has been discontinued almost completely.

It should be pointed out that the careful use of specifically indicated antibiotics may be lifesaving in patients who have developed septicemia but that, in the local care of the burn wound, antibiotics have contributed very little. Surgical cleanliness in the care of the wound is more important than the use of antibiotics to control surface infection of the burned area, where infection has taken place because of inadequate cleanliness.

John Rhea Barton Professor of Surgery, Hospital of the University of Pennsylvania Department of Surgery.

Specific Measures

Widespread claims have been made for a variety of locally applied agents concerning their ability to accelerate nature's processes of healing; however, the most exacting studies have failed to fulfill the claims made for any of these agents. After careful study, the innumerable substances which have been advocated for local use have proved to be of little practical value. In fact, many of the agents which have been used to promote healing have been shown to be detrimental to epithelization.

Enzymatic débriding agents have been advocated by several investigators, but, in spite of impressive laboratory work, they have not proved to be very effective in man. The best method of cleaning the burned area, if this is necessary, is still by washing with surgical soap and sterile water or physiological saline solution. The best débridement is still achieved by time or the surgeon's scalpel, and the best dressing is still a fine-mesh gauze lightly impregnated with an innocuous bland ointment.

The only worthwhile place for a specialized burn ointment (if such an ointment exists) seems to be on a small superficial burn for the immediate relief of pain. Even so, burn wounds are seen daily which have had no mechanical cleansing and which are badly infected, in spite of the generous application of some proprietary ointment. History has repeated itself over the centuries.

Clinical studies have shown clearly that, in third degree burns, rapid healing is best obtained if the granulating surface and surrounding skin are kept meticulously clean with soap and water, plus the frugal use of ether or benzene for the removal of keratin scales and macerated tissues. Skin grafting is faster than any known therapeutic agent in providing coverage for areas of deep burns, reducing the bacterial flora of a wound, and restoring the critically burned patient to good health. Frequent blood transfusions, light safe anesthesia, and nutritional adjuncts given intravenously or orally have added greatly in reaching this goal. The best means of providing adequate calories is by mouth. This method should always be used if possible. Intravenous alimentation should be used to increase oral caloric intake, if this is inadequate.

Progress in the treatment of burn shock has been great, and, if it is treated early, the large majority of severely burned patients can now be brought successfully through this phase of their injury. Several formulas have been proposed as guides for the administration of fluid during the shock phase. At times, too much fluid is given, and pulmonary edema is produced. One cause of overhydration is overestimation of the area burned. Less than the estimated volume of fluid should be given to children, elderly patients, those with serious heart disease, those with respiratory burns, and those with more than 40% of burned body surface. Each patient's response must be closely observed and his therapy adjusted accordingly. The use of an indwelling catheter in the urinary bladder enables one to follow closely the rate of formation of urine and is helpful in judging the adequacy of intake. Urine formation of 25 to 50 cc. an hour is a satisfactory rate, but fluid therapy should not be gauged on this factor alone.

Contrary to the prevailing opinion of a decade ago, it is now believed that large quantities of salt may be necessary in the early phase of treatment because of the rapid fall in the level of serum sodium. Associated with the rapid drop in serum sodium, there is a period of sodium retention usually lasting several days. After the period of retention, the kidneys usually excrete a large amount of fluid and sodium, unless severe renal damage exists. If the salt solution can be given orally, a weaker solution not only is better tolerated but also obviates the necessity of giving the extra water intravenously. The more severely burned patients, however, often cannot tolerate fluids given by mouth.

The rapid loss of plasma from the burned surface and into the tissue beneath the burn has long been recognized, and, until recent years, plasma alone has been considered the proper colloid with which to combat this loss. Recent evidence indicates that whole blood is also needed in burn therapy. Whole blood is needed not only to prevent anemia, long observed to occur several days after burning, but also to replace the red blood cells that are destroyed after burning. Determination of hemoglobin and hematocrit levels gives no indication of this loss and cannot serve as a reliable guide for the volume of whole blood needed.

One of the most striking changes in burn therapy in recent years has been the more frequent acceptance of the open method of treatment. From the reports of several excellent investigators, it appears that the open method can be used with equally good results in some patients. The open treatment is not a treatment of neglect but a method which requires skill and a thorough knowledge of the principles of wound healing. This treatment must not be used for granulating surfaces. Some of its advocates do not advise its use for burns of the flexor surfaces of the neck, for circumferential lesions of the trunk, and for burns on the surfaces of joints of the legs and arms.

General agreement exists that full-thickness burns should be excised and the defect grafted as soon as this is feasible. Early excision and grafting shortens the period of protein loss from burned surfaces, diminishes infection and toxic absorption, and reduces scar formation. Immediate excision and grafting, however, may be prevented by the general condition of the patient, which may make additional trauma too hazardous, and the difficulty of immediately judging the depth of the burn. In burns of limited extent that are obviously full-thickness burns, early excision and grafting is the best treatment. In the patient with extensive burns, the additional trauma of anesthesia and operation may be contraindicated in the early stages of the burn. Excision of dead skin, however, once carried out, will improve the patient's condition at any stage. It is then a question of balancing these two factors with the fact that obvious full-thickness burns should be excised and grafted as soon as the patient can stand the operation. If the normal skin of the patient is insufficient for grafting or if the added trauma of taking a graft is felt to be unwarranted, homologous skin can be used to cover the wound as a temporary expedient. Because grafted skin is usually inferior to superficially burned skin that has regenerated, the ultimate result may be better if, in questionable cases, time is given for demarcation before skin is excised.

The early hope that corticotropin and cortisone might effect a permanent "take" of homologous skin has been shown to be ill-founded. In extensive burns, especially in children, the temporary covering of the open wound with homologous skin may be lifesaving, even though subsequent replacement with the patient's own skin is necessary.

Comment

It is hoped that in the future we can look forward to better ways of distinguishing superficial burns of first or second degree from deep burns of third degree. It is hoped, too, that we will achieve a better understanding of the "toxic" phase of a burn. Perhaps we shall find better débriding agents with a higher specificity for necrotic tissue, and, perhaps, better agents to stimulate epithelization. In spite of the development of many potent antibiotics, sepsis continues to plague the severely burned patient. All too frequently the patient survives burn shock, the toxic manifestation of the injury, and the early phases of treatment, finally dying from sepsis after several weeks. Local agents to control pain are no longer used. Gentleness in the care of the patient and early removal of necrotic skin, with early grafting, provide the best means of making the patient comfortable.

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COMMITTEE ON REHABILITATION

The following report is the second in a series of articles which have been authorized for publication by the Committee. The first appeared in the Oct. 24 issue of THE JOURNAL, *page 1107. This series deals with various aspects of rehabilitation which are of interest to physicians.*

RALPH E. DE FOREST, M.D., *Secretary.*

TRAINING IN PHYSICAL MEDICINE AND REHABILITATION

Charles D. Shields, M.D.
and
Hugh H. Hussey, M.D., Washington, D.C.

Rehabilitation is a word that denotes restoration or improvement in condition. In medicine it is concerned with a type of practice which places broad social responsibilities on the physician. Physical medicine and rehabilitation is directed toward treatment of disability. It is concerned not only with medicine but with social, educational, and vocational opportunities for patients. The services of nurses, therapists, counselors, and teachers are utilized. The dedicated assistance of these coprofessional groups has done much to elevate standards of medical care. Individuals preparing themselves for medical practice today must be taught the methods and techniques of rehabilitation, along with their obligations and responsibilities to the numerous allied groups with whom they are associated in practice.

A New Medical Responsibility

The United States Army, in World War I, developed methods to shorten convalescence, provide vocational training, and return the soldier to work or to the highest level of self-care.[1] To accomplish this, a Division of Special Hospitals and Physical Reconstruction was formed in the Office of the Army Surgeon General in August, 1917. Excellent plans were developed for the care of the disabled. The Armistice of November, 1918, resulted in demobilization of trained medical personnel and in failure of this effort. During World War II, our present attitudes toward rehabilitation as a concept of medical practice were developed. The specialty of physical medicine and rehabilitation was organized to supervise and coordinate the work of various types of therapists and counselors in the care of neuromuscular diseases and certain musculoskeletal defects. This also provided diagnostic facilities, direct medical supervision, and continuous medical evaluation. Since the war, the scope of rehabilitation has developed and expanded, often under the leadership and insistence of lay groups. We must remember that the present status and usefulness of preventive medicine, public health, and psychiatry resulted from lay demands and not from any great foresight on the part of the medical profession. In the case of rehabilitation medicine, we must look beyond the immediate horizon and plan for the future, or once again we will suffer the embarrassment of doing the job after we have been pushed into position. Physicians as citizens have a great economic stake in the national rehabilitation program. During the history of our nation, when accident or disease resulted from military service and in more recent years from employment, full medical coverage has been regarded as the right of the patient. When he is not returned to a prior level of fitness, he is considered eligible for pension benefits. We cannot afford to have less than complete and superior rehabilitation services. These are, in the last analysis, a real economy. The techniques must be developed and improved by practice and research and properly taught to students in the health professions.

Teaching Rehabilitation to Medical Students

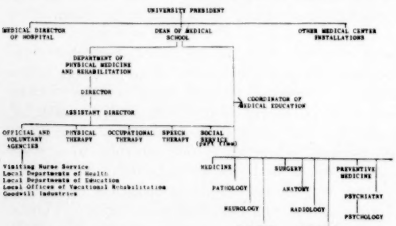
It is essential that a teacher understand for what he is preparing his students and that he have a plan or method to accomplish this goal. There is no "best method" or "only way." We believe that physical medicine and rehabilitation, under certain circumstances and in certain areas, should be practiced by competent specialists and, under all conditions, should be available to every physician engaged in any type of practice within the limits of his training, interest, and equipment. Physical medicine and rehabilitation is a medical specialty concerned with the management of patients who have disabilities that may benefit from physical diagnostic procedures, physical treatment, and broad rehabilitation services.

Georgetown University School of Medicine has recently developed a comprehensive rehabilitation program (see figure). Physical medicine and rehabilitation is taught in the second, third, and fourth years. Physical medicine is presented as a

Professor and Chairman, Department of Physical Medicine and Rehabilitation (Dr. Shields) and Dean, Georgetown University School of Medicine (Dr. Hussey).

special field of practice concerned with the diagnosis and treatment of neuromuscular diseases and certain musculoskeletal defects. Rehabilitation is presented as a complex responsibility that affects all departments in the medical school.

The department of physical medicine and rehabilitation has the status of a major department and directs and coordinates the total program. It is represented on the executive faculty by the chairman of the department. It is concerned with the presentation of material to students that will acquaint them with the specialty and with the obligations of the physician to obtain, for certain of his patients, services that are beyond the confines of individual medical practice. The student is impressed in this manner with his obligation to assume responsibility for return of his patient to the vocation of his choice or to the highest level of self-care consistent with the residuals of his illness or injury. Case presentations, seminars, and conferences are the usual techniques of teaching the subject. These are frequently interdepartmental,



Organizational plan for teaching physical medicine and rehabilitation, Georgetown University School of Medicine, Washington, D. C.

with members of coprofessional groups participating. In this manner, integrated and coordinated medical care is demonstrated, as well as the relationship of nurses, therapists, and counselors to the physician. The student is introduced not only to his medical responsibilities in this area but also to his direct advisory functions to the social, educational, and vocational services essential to the welfare of the patient.

Techniques and methods must be demonstrated as well as discussed with students. Departments of physical medicine and rehabilitation must, therefore, be developed to a reasonable standard of excellence to provide the means for this accomplishment. This is an expensive effort, and personnel are not always readily obtainable. Medical leadership is necessary to furnish diagnostic and evaluation services along with direct supervision of coprofessional groups. In our department of physical medicine and rehabilitation, physical therapy, occupational therapy, and speech therapy are established as sections. A prevocational testing laboratory emphasizes clerical skills. Social service is available on a part-time basis. Psychological services are obtained through the department of psychiatry. There are direct and pleasant relationships with all other school and hospital departments and with outside official and voluntary agencies.

The department of physical medicine and rehabilitation was established at Georgetown University in 1954. At this time, the department was assigned responsibility for eight lectures to the junior class and for training senior clerks who were assigned to the University Hospital service. This effort was a resounding failure because a department must be well established before it can serve in an effective manner for teaching purposes. Physicians properly trained in the specialty are scarce. When one or two are available and are engaged in a busy hospital practice establishing and operating a service, they have little time to associate themselves with the clerkship method of instruction. After consideration of the problem, it was decided to join the older and well-established departments, to utilize their conferences, seminars, and, on occasion, ward rounds, in order to present the fundamentals of rehabilitation medicine. These difficulties may have stimulated a new method of teaching now in use at our school, characterized by fewer lectures and increased number of interdepartmental conferences.

The cost of instruction in physical medicine and rehabilitation at Georgetown University is augmented by a training grant from the Office of Vocational Rehabilitation. The teaching program is as follows:

Second Year.—During the second year the department of physical medicine and rehabilitation takes part in teaching activities as follows:

Preventive Medicine: In the teaching of preventive medicine, the idea of directing the activities of coprofessional groups is developed. For example, a social worker presents a request received from the physician and then discusses the results of her interview and evaluation; a physical or occupational therapist reads the prescription of the physician and demonstrates by use of a patient the methods by which she approaches the goal of therapy.

Physical Diagnosis: In the teaching of physical diagnosis, material is presented concerning the evaluation of weakness and methods of grading and recording muscle weakness, fascial tightness, and measurement of joint range of motion.

Conferences on Mechanisms of Disease: During the second semester of the sophomore year, 68 conferences on the mechanisms of disease are conducted. The department of physical medicine and rehabilitation takes part in certain of these conferences. Two of these are musculoskeletal trauma, in which general surgery and orthopedic surgery are the other participants, and disorders of muscle, in which the departments of pathology and neurology participate.

Third Year.—During the third year there are 128 conferences on diagnosis and treatment, each lasting two hours. The department of physical medicine

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and rehabilitation is represented in 16 of these interdepartmental activities. Because the emphasis here is on diagnosis and treatment, methods of using therapist and counselor services are frequently presented, in addition to methods and indications for therapy.

Fourth Year.—During the fourth year the department of physical medicine and rehabilitation shares teaching beds with the department of neurology. Senior clerks are assigned to this service. On one day each week, a member of the department of physical medicine and rehabilitation conducts the rounds and emphasizes therapy and rehabilitation rather than diagnosis. This method is of mutual advantage to the departments of neurology and physical medicine and rehabilitation. Members of the department of physical medicine and rehabilitation take part in ward rounds conducted by other departments on request. It is our experience that this teaching schedule taxes the capacity of two full-time teachers who also operate the department of physical medicine and rehabilitation in the University Hospital.

Training Residents in Physical Medicine and Rehabilitation

Physical medicine and rehabilitation is a broad specialty that offers varied fields of interests to the resident and one which requires much cooperation from many departments in the medical school and hospital. A minimum of three years of residency training is considered necessary to train a physician who desires to specialize in this field. During this period, instruction at the graduate level in anatomy, physics, biophysics, and pathology is essential. Special courses in these sciences are arranged as follows:

1st Year of Residency:

Anatomy

Neuroanatomy—4 semester hours, lectures 2 hours per week, laboratory 4 hours per week (one semester).

Anatomy—Musculoskeletal system, 2 semester hours arranged with the department of anatomy in regular courses of instruction in the medical school.

Physiology

Neuromuscular Physiology—2 semester hours.

Physiology of Respiration—2 semester hours. These courses are arranged with the department of physiology in the medical school.

2nd Year of Residency:

Physics—2 semester hours.

Biophysics—2 semester hours. Presented by personnel in the department of physical medicine and rehabilitation.

All Years of Residency:

Pathology—Residents attend all death conferences.

Clinical aspects of training are presented in the usual graded manner, with gradually increasing responsibility for patient care. It is therefore essential that teaching beds be provided for this purpose. At Georgetown University Hospital, 20 beds are shared with the department of neurology. Again, in teaching residents, there is a close relationship between these two departments.

Residents are obliged to attend all conferences and ward rounds of the departments of physical medicine and rehabilitation and neurology as well as medical and surgical grand rounds. Residents in physical medicine and rehabilitation are assigned for specific training purposes for short periods to the departments of medicine, neurology, surgery, anesthesiology, psychiatry, and physiology. During these assignments, they are under the direct supervision of the department of physical medicine and rehabilitation and are absent only for specific training purposes and not for routine assignment. This is to provide continuous, concentrated, and supervised training in the special field of physical medicine and rehabilitation and to prevent mere utilization of residents' services by other departments.

Arrangements are made for the second-year and third-year residents to assume increasing responsibility for outpatients and to spend time in voluntary and official agencies under proper medical and other appropriate supervision to observe social, educational, and vocational services for the disabled. It is our opinion that adequate practice facilities must be provided by affiliation. The resident is assigned for certain periods of time to a psychiatric rehabilitation service, a tuberculosis rehabilitation service, an official vocational rehabilitation agency, a cerebral palsy center with complete services, and an educational program with rehabilitation services.

We are firm in our opinion that physical medicine and rehabilitation cannot be taught to residents isolated from other special interests in medicine. It must be a major activity within the hospital. Residents in physical medicine and rehabilitation are taught important fundamentals in other medical specialties. This insures that residents in other specialties will develop knowledge concerning physical medicine and rehabilitation and will learn to use and respect it accordingly. The resident in physical medicine and rehabilitation thus develops the broad foundation upon which success of his training depends. He will, at the same time, learn his own limitations and those of his special field in medicine.

Summary and Conclusions

Medical school curriculums should include provision for instruction in the field of physical medicine and rehabilitation. A method of teaching this subject to medical students considers availability of limited numbers of trained teachers, utilizes existing facilities of other departments in the school, and creates a high level of mutual understanding among members of the faculty. Development and expansion of the specialty of physical medicine and rehabilitation demand that young physicians become interested and trained in the specialty. Instruction of residents in this area of medicine provides broad training in a field of wide responsibility and considers economy of personnel, space, and equipment.

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TRAINING FOR TOMORROW

IN NO area of medical instruction is there a greater need for long-range vision than in the department of internal medicine in a teaching hospital allied with a medical school. Such a department, responsible for medical training in its broadest sense, may be expected to define and to implement the pattern of conduct for other departments to follow in the clinical sciences. One may inquire justifiably, why it is necessary to establish a pattern of conduct for the future when our medical schools and teaching hospitals are credited with performing a thoroughly commendable job at the present time. It is not necessary to search deeply to discover the answer. Although the obvious is not appreciated widely, and hence lacks the general recognition that it deserves, the absorption and comprehension of medical knowledge available today by young physicians in training does not automatically insure continued ability to absorb and to comprehend the medical knowledge that will become available tomorrow. Equal in importance to the task of communication of the latest and best of today's information must be the keen awareness of what is not yet discovered and that, when it is revealed at some future time, the physician in practice will be prepared to digest and to assimilate the new. Only with such a philosophy will the patient continue to be the recipient of the best medical care.

The responsibility for the direction of training today and the planning for tomorrow resides largely in the faculties of our medical schools. To be sure, medical associations, research foundations, and the National Institutes of Health contribute immeasurably: agencies and institutions which should work hand in hand with the teachers and officers of the medical schools. The volume of clinical problems, the magnitude of investigations in progress, and the size of the professional groups places the department of internal medicine in a foremost position in the medical faculty. Thus the pattern of conduct for such a department becomes crucial. Dr. Walter Bauer, Jackson Professor of Medicine at Harvard Medical School, has presented a clear narrative of the program at the Massachusetts General Hospital for the training of medical students, interns, research fellows, training fellows, and graduate students in the broad field of internal medicine. A description of the fundamental precepts of the training program was presented in the Presidential Address at the annual meeting of the Association of American Physicians in Atlantic City, May 5, 1959. The address appears in this issue of THE JOURNAL (page 1277).

The address is an exposition of a highly imaginative and effectively coordinated protocol of group responsibility. Concentration within the field of internal medicine is considered vital. Basic scientists actively participating in the training of physicians in clinical departments as well as advancing the frontiers of knowledge by means of isotopes, electrophoretic patterns, and exploration of enzyme systems are integral components of the group. Qualified volunteer physicians have an equally vital assignment within the corporate structure. A pattern of conduct such as that in effect at the Massachusetts General Hospital is not the only instrument to insure a successful goal. Other medical faculties are exploring diverse ways and means to accomplish similar objectives. The MGH plan is deemed worthy of examination, however, in order that the primary purpose of the teaching hospital, i. e., the care of the sick, be fulfilled. This is best achieved by advancing knowledge through research in their own laboratories, utilizing knowledge disseminated from other laboratories, and finally by accepting the concept that contemporary medical training must be imaginative as well as profound in order that the physician in training today will continue to provide the best care and service to the person who becomes a patient tomorrow.

CHANGE OF ADDRESS

If you change your address please notify THE JOURNAL at least six weeks before the change is made. Include the address label clipped from your latest copy of THE JOURNAL, being sure to clearly state both your old and new address. If your city has Postal Zone Numbers, be sure to include this Zone Number in your new address.

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COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

On recommendation of the Residency Review Committee for Obstetrics and Gynecology, its three sponsoring organizations, the American Board of Obstetrics and Gynecology, the American College of Surgeons, and the Council on Medical Education and Hospitals of the American Medical Association have adopted the following principles of residency approval in this specialty. Recommendations one through nine deal with matters of procedure within the Committee; recommendations 10 through 13 represent changes in policy which are in accordance with the "full training" concept of graduate education. The attention of physicians participating in residency programs in this specialty is called to the fact that after July 1, 1962, residency programs not including, either intramurally or through affiliation, 36 months of clinical training in obstetrics and gynecology, will no longer be approved.

WALTER S. WIGGINS, M.D., *Secretary.*

RESIDENCY TRAINING IN OBSTETRICS AND GYNECOLOGY

1. Reports of the field staff on residency programs are distributed by the Secretary to Committee members for review prior to each meeting; these reports are then considered by the Committee as a whole at the next meeting and appropriate action taken. An *ad hoc* committee may be appointed to act for the Committee in such instances as are designated.

2. After reviewing a program, the Committee may approve, provisionally approve, disapprove, defer action, or place program on probation. In the event of an action other than approval, specific reasons for such action are to be stated in the letter of notification.

3. When approval is granted, this approval is considered retroactive to the beginning of the current year of service for any resident on duty, or to the date of application for approval, whichever date is earlier.

4. When a training program does not meet the requirements for continuation of approval, but has the potential for doing so, that program may be placed on probation until requirements are met. A period of 12 to 18 months is allowed for correction of deficiencies. If correction has not been accomplished by the specified date, appropriate action will be taken.

5. When a training program is not yet in full operation but shows promise of meeting all educational requirements, the program may be granted provisional approval, subject to early review.

6. When a previously approved training program cannot meet requirements, the effective date of withdrawal of approval, after fair warning, shall be determined by the Committee.

7. Routine surveys of residency training programs will be made at periodic intervals by the field staff of the Council.

8. The Committee can, at any time, request reinspection of a program by either a member of the Council field staff or a regional evaluator representing the Committee. The Council shall be responsible only for expenses incurred by its field staff in making such inspection. The expenses incurred by the regional evaluators shall be borne by the other sponsoring organizations.

9. Listing of approved programs in the Internship and Residency Number of THE JOURNAL of the American Medical Association shall be the responsibility of the Council, and listing in the *Bulletin of the American College of Surgeons* shall be the responsibility of its Board of Regents.

10. Beginning July 1, 1962, one-year programs approved only for the first year in obstetrics and/or gynecology will not be approved and the institutions involved are urged to affiliate with programs offering full training. In the programs offering affiliation, approval will be given only to the parent program.

11. Two-year residency programs in obstetrics and gynecology will not be approved after July 1, 1962. Institutions offering two-year programs are encouraged to expand to three years or affiliate with a full program.

12. Two-year residencies in gynecology only and in obstetrics only will not be approved after July 1, 1962. They should affiliate to produce a program which can be approved.

13. While training in general surgery, internal medicine, and urology is desirable, such training should not be a part of the three years' required clinical program in obstetrics and gynecology. A minimum of 18 months in obstetrics and 18 months in gynecology is required. Likewise, formal courses in the basic sciences which separate the resident from clinical training should not be included in the three-year minimal clinical training program.

COUNCIL ON NATIONAL DEFENSE

COURSES ON MANAGEMENT OF MASS CASUALTIES

The following dates for civilian physicians to attend Management of Mass Casualties courses at Army Medical Service School, Brooke Army Medical Center, Fort Sam Houston, San Antonio, Texas, are still open: Nov. 30-Dec. 4, 1959; Feb. 15-19, 1960; April 25-29, 1960; and June 13-17, 1960. There are spaces for two civilian physicians for each of these scheduled courses, except that of Feb. 15-19, 1960, for which one space is still open. These quotas are made available to the A. M. A. Council on National Defense by the Office of the Surgeon General, Department of the Army. Physicians interested in attending are requested to write directly to the Council on National Defense.

PUPIL SAFETY IN DISASTER

With the cooperation of the Office of Civil and Defense Mobilization, the American Association of School Administrators has published a pamphlet for school administrators who are developing school disaster protection programs. Entitled "Disaster Protection Handbook for School Administrators," the emphasis is on pupil safety under disaster conditions. Copies may be obtained from OCDM.

GOVERNMENT SERVICES

NAVY

Defense Course.—A four-weeks' course in ABC (atomic, biological, and chemical) warfare defense, for active duty medical department officers possessing security clearance, will convene at the U. S. Naval Schools Command, Treasure Island, San Francisco, Calif., on Jan. 4, 1960. A class quota of 50 has been assigned. Ten spaces will be reserved for Army and Air Force officers. The breakdown for the Navy will be 30 Medical Corps, 5 Dental Corps, and 5 Medical Service Corps officers.

During the course the medical aspects of modern warfare and of military peacetime operations including problems incident to atomic, biological, and chemical weapons systems, nuclear propulsion, mass casualties, and isotope programs will be stressed. Military aspects of the weapons systems and military countermeasures will also be considered so that medical officers may function effectively on a staff and can reasonably assess the medical compromises imposed by the military situation. Outstanding speakers, both military and civilian, will be featured on the program. Visits will be made to the Navy Radiological Defense Laboratory and the Naval Biological Laboratory, as well as practical exercises and drills. All students will be supplied textbooks on a permanent retention basis.

Eligibility for Navy officers is as follows. 1. Requests for attendance are invited from medical officers; reserve officers of the Medical Corps whose attendance would obviously assist them in the performance of their duties will be considered providing they have a minimum of 20 months of obligated service remaining. 2. The dental officers to attend will be selected by the bureau of medicine and surgery. 3. Requests are invited from senior Medical Service Corps officers. Priority will be given to officers assigned duties on fleet and/or district staffs, and administrative officers of Naval hospitals. Interested officers with the foregoing requirements must submit a written request via their commanding officers, to reach the bureau of medicine and surgery (Attn: code 316), prior to Nov. 15, 1959.

Personal.—Capt. Paul R. Engle recently reported to the bureau of medicine and surgery for duty as deputy director, physical qualifications and medical records division.——Rear Adm. J. L. Holland, M. C., assumed command of the Naval Aviation Medical Center, Pensacola, Fla., in September. He is the first flag officer of the Navy Medical Corps ever to serve on active duty in Pensacola.

VETERANS ADMINISTRATION

Computer for Cardiac Diagnosis.—An electronic data computer for the study of heart disease was developed by a Veterans Administration–National Bureau of Standards research team consisting of Leonard Taback, Ethel Marden, H. L. Mason, Dr. Hubert V. Pipberger, and Dr. Edward D. Freis. Electrical impulses from the heart are recorded, converted to a numerical system, and fed into an electronic computer, which is set up to provide the physician with quantitative data on major char-

acteristics of the heart. The device appears to promise more complete information than has been available from the electrocardiogram and also to be economically feasible for wide use.

Award to Dr. Lyon.—The Veterans Administration has given its highest award, the Exceptional Service award, to Dr. George M. Lyon, for his pioneering work in atomic medicine. In presenting the award the administrator of Veteran Affairs, Sumner G. Whittier, said:

"Recognizing the tremendous potential of atomic force for good and harm, Dr. Lyon became an active participant in the study of its biologic and medical applications. Under his energetic guidance, the Veterans Administration became a leader in the application of radioisotopes to research, diagnosis, and treatment. Its record of safety in this virgin field has been a model for similar enterprises. The monitors trained under this program will be an invaluable asset in the event of nuclear attack or accident."

Medical Advisory Group.—Five new members have accepted appointment to the Veterans Administration special medical advisory group. The group meets quarterly to advise the Administrator of Veterans Affairs and the VA Chief Medical Director on the VA medical program. The new members, four of whom are replacements for former members whose terms have expired, are (1) Dr. Jasper L. Callaway, professor of dermatology and syphilology at Duke University, who replaces Dr. Clarence S. Livingood, chief of the dermatology department of Henry Ford Hospital in Detroit; (2) Dr. Arthur G. DeVoe, professor and chairman of the department of ophthalmology of New York University Post-Graduate Medical School and director of eye service at Columbia University Hospital, who replaces Dr. Harold G. Scheie, professor of ophthalmology at the University of Pennsylvania; (3) Dr. Raymond J. Nagle, dean of the College of Dentistry of New York University, who replaces Dr. Clemens V. Rault, dean of Georgetown University School of Dentistry; (4) Dr. Ralph M. Tovell, director of the department of anesthesiology of the Hartford (Conn.) Hospital, who replaces Dr. Donald E. Hale, head of the anesthesiology department of the Cleveland (Ohio) Clinic Hospital; and (5) Dr. O. Currier McEwen, associate professor of medicine at New York University and formerly chief consultant in medicine in the European theater of operations during World War II, who replaces Dr. Richard P. Stetson, who resigned from the special medical advisory group to become area director of professional services in the Boston VA area medical office.

Personal.—Dr. Martin M. Cummings, director of medical research for the Veterans Administration in Washington, D. C., left the VA in October to become chairman of the department of microbiology at the University of Oklahoma School of Medicine in Oklahoma City. He will continue to be affiliated with the VA as a consultant to the agency's Oklahoma City Hospital, where he also will do research on sarcoidosis.

U. S. Contributes to Malaria Eradication.—Dr. Leroy E. Burney announced that the United States will contribute 2 million dollars to the Pan American Health Organization's malaria eradication campaign in 1960. This makes the United States total contribution to this PAHO fund $8,500,000 since 1956. The United States will also make a contribution of 3 million dollars to the Special Malaria Eradication Account of the World Health Organization.

PUBLIC HEALTH SERVICE

Limitation of Activity.—Chronic conditions affecting health limit the normal activity of an estimated 17 million people in the United States, according to findings developed from nationwide household interviews conducted by the Public Health Service. The information recorded about individual persons is confidential, and only statistical totals are published. These 17 million persons, representing 10% of the population, are limited in their ability to work, keep house, or pursue outside activities. A segment of this group amounting to 3% of the population or an estimated 4,855,000 persons have trouble moving about or cannot move about without help. Of the latter group, about 1 million persons are completely confined to their homes. The figures do not include military personnel or people in mental or other types of long-term institutions.

Activity limitations were reported most frequently among low income families and older people. Among families with incomes of less than $2,000 a year, 20% had some activity-limiting condition; for those with incomes of $7,000 or more, only about 7% were similarly limited. About 1.4% of the children under 15 years of age have some activity limitation, whereas about 50% of the persons 75 years of age and older fell in this category. The report is entitled "Limitation of Activity and Mobility Due to Chronic Conditions, United States, July 1957-June 1958," Public Health Service Publication no. 584-B 11. Copies may be obtained from the Superintendent of Documents, Government Printing Office, Washington 25, D. C., at 30 cents each.

Study on the Stein-Leventhal Syndrome.—An investigation of the role of the adrenal gland in the Stein-Leventhal syndrome has been initiated at the Clinical Center, National Institutes of Health. Salient features in this syndrome include oligomenorrhea, hirsutism, and polycystic ovaries. The cooperation of interested physicians in referring laparotomy-proved cases is invited. Referral letters will receive prompt attention and should include detailed medical information about the patient. Accepted patients will be studied for varying periods up to several weeks. On completion of their study, patients will be returned to the care of their referring physician, who will also receive a detailed report. In some instances it may be desirable to arrange for occasional follow-up visits to the clinical center. These would supplement rather than substitute for visits to the patient's own physician.

Physicians interested in the possibility of referring patients should write to (1) J. E. Rall, M.D., chief, clinical endocrinology branch, National Institute of Arthritis and Metabolic Diseases, Bethesda 14, Md., or (2) Saul W. Rosen, M.D., clinical associate, National Institute of Arthritis and Metabolic Diseases, Bethesda 14, Md.

Personal.—Dr. Donald Roger Chadwick of the Public Health Service was appointed as secretary of the Federal Radiation Council.—Dr. Robert W. Wilkins, of Boston, was appointed to the National Advisory Heart Council for a four-year term. He is one of the world's foremost authorities on hypertension.—Dr. Joseph A. Gallagher was appointed to the headquarters staff of the division of Indian Health of the U. S. Public Health Service in Washington, D. C. He moves to Indian health headquarters as a member of the staff in hospital administration after three years as medical officer in charge of the division's Alaska Native Health Service Area office at Anchorage.

NATIONAL SCIENCE FOUNDATION

Graduate Awards.—Applications are being accepted for National Science Foundation Graduate Fellowship awards for advanced study in the sciences, including medicine. Fellows will be selected on the basis of ability as attested by letters of recommendation, academic records, and other evidences of attainment. Applicants must take the graduate record examination. Applicants' qualifications will be evaluated by carefully chosen panels operating under the aegis of the National Academy of Sciences–National Research Council. Stipends for these fellowships vary with the academic status of the fellows. First-year fellows (students entering graduate school for the first time or those who have had less than one year of graduate study) will receive annual stipends of $1,800. Fellows who need one final calendar year of training for the doctoral degree will receive annual stipends of $2,200. Fellows between these two groups will receive stipends at the rate of $2,000 annually. A dependency allowance of $500 per annum for spouse and for each dependent child will normally be available to married fellows. Tuition, laboratory fees, and limited travel allowances will also be provided.

Application material for the graduate fellowship program may be obtained from the Fellowship Office, National Academy of Sciences–National Research Council, 2101 Constitution Ave., N. W., Washington 25, D. C. The closing date for the receipt of applications is Jan. 1, 1960. Final selection of fellows will be announced March 15, 1960.

FOOD AND DRUG ADMINISTRATION

Bust Developers.—Mechanical contrivances for increasing the size of women's breasts are a swindle and a potential hazard to health and are considered illegal per se. The Food and Drug Administration seized one make of these devices at Tampa and Clearwater, Fla., and Phoenix, Ariz. The seized devices, involving an electric air pump and plastic suction cups, were alleged to be dangerous to health and to be misbranded by false and misleading labels claiming to increase the size and firmness of the breasts.

Colored Light Not a Cancer Cure.—Exposing the body to colored light will not cure cancer or any other serious disease. The Food and Drug Administration seized component parts for color lamps promoted with cure-all health claims. The promoter sold the device in do-it-yourself assembling kits, consisting of a lamp base, electrical fixtures and wiring, and plastic slides in a set of five colors. The promoter, in his literature, offered the device as a cure for leukemia, tumors, glaucoma, arthritis, rheumatism, bursitis, neuritis, anemia, asthma, tuberculosis, all diseases of the eye, nose, and throat, measles, whooping cough, scarlet fever, influenza, and all diseases which may affect the body of man.

Voluntary Actions by Food and Drug Firms.—Improvements costing nearly 4 million dollars were made voluntarily by food and drug manufacturers and warehousemen in the fiscal year 1959 to aid in protecting consumers. In addition, 8,000 tons of unfit foods and $176,000 worth of substandard drugs were removed from the market in 1,228 voluntary actions. This report covers only those actions observed by or reported to Food and Drug Administration inspectors. Many similar actions were undoubtedly taken by other firms and did not come to official notice. Voluntary corrections included improvements of plant sanitary conditions, improvement of processing and storage practices, and disposal of unfit products.

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MEDICAL NEWS

ALABAMA

Heart Center Dedicated.—Dedication of the University of Alabama Medical Center's cardiovascular unit to the memory of the late Dr. Luther Leonidas Hill Jr., pioneer Alabama surgeon, was held Oct. 18. Events included the dedication ceremony, a reception for invited guests, and a tour of the Luther Leonidas Hill Heart Center. Among those participating were Sen. Lister Hill, son of Dr. Hill and senior U. S. Senator from Alabama. Dr. Luther L. Terry, senior investigator and assistant director of the National Heart Institute, Bethesda, Md., was the featured speaker. A namesake of the late Dr. Hill, Dr. Terry is from Red Level. Dr. Luther Leonidas Hill, who practiced in Montgomery for nearly half a century, was the first physician in America to report a successful suture of the human heart. He performed this operation in 1902 on a 13-year-old boy who had received a stab wound penetrating the left ventricular cavity. Dr. Hill was elected president of the Medical Association of Alabama in 1897.

CALIFORNIA

Dr. Geiger Honored.—At a banquet Sept. 5 the "Distinguished Service" silver scroll with bronze coat of arms medallion of the Pan American Medical Association was presented to Dr. Jacob C. Geiger, San Francisco.

COLORADO

Scholarship to Aid Medical Students.—The Denver Medical Society announced the establishment of a $100,000 scholarship fund to aid "gifted and deserving medical students" at the University of Colorado School of Medicine, Denver. Dr. Carl A. McLauthlin, chairman of the society's board of trust, said the fund was made possible by the gift of $100,000 from Miss Grace Isabelle McNaught in memory of her father, Dr. Francis H. McNaught, after whom the fund will be named. Dr. McNaught was a professor of operative obstetrics in the University of Colorado School of Medicine and was the only Colorado doctor ever to serve as president of the Colorado State Medical Society for two years. The fund will be administered by the trustees of the medical society.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

CONNECTICUT

Lecture on Schizophrenia.—The Yale Medical Society will present "Current Biochemical Theories of Schizophrenia" by Dr. Seymour S. Kety, chief, Laboratory of Clinical Science, National Institute of Mental Health, Bethesda, Md., on Tuesday, Nov. 10, 5 p. m., in Fitkin Amphitheater, at the Yale–New Haven Medical Center, New Haven. Physicians on call should leave the number LOcust 2-1161, Ext. 865.

GEORGIA

Conference on Nutrition.—The second "Better Foods for Better Nutrition Conference," a joint conference sponsored by the divisions of foods and nutrition and food processing of the University of Georgia, will be held March 3-4, 1960, at the Center for Continuing Education, University of Georgia, Athens. This conference is planned for persons engaged in research, extension, and teaching of foods and nutrition or food technology, as well as home economists in business, lunchroom supervisors, hospital dieticians, public health nutritionists, and handlers and processors of foods. Special attention will be given to industrial and institutional problems in processing, handling, and serving foods. For information, write John J. Powers, Ph.D., Head, Department of Food Technology, College of Agriculture, University of Georgia, Athens.

ILLINOIS

Hospital News.—On Sept. 3, Dr. T. B. McMurry, of the University of Capetown, South Africa, addressed the weekly staff conference in orthopedic surgery at Hines Veterans Administration Hospital. His subject was "Recurrent Dislocation of the Shoulder."——Forest Hospital, Des Plaines, appointed Dr. Kalman Gyarfas, Chicago, as consultant of the psychiatric training program. Dr. Gyarfas will help to plan and implement a training program for nonpsychiatric interns and residents in the community. He will also serve as consultant on the hospital's other educational programs and for its research programs.

Chicago

Dr. Visotsky Named Mental Health Director.—Dr. Harold M. Visotsky, assistant professor of psychiatry, University of Illinois College of Medicine, was appointed director of mental health for the City of Chicago. He will head the program of the mental health section of the Chicago Board of

Health under Dr. Herman N. Bundesen, president. His appointment became effective Sept. 1. Dr. Visotsky succeeds Dr. Henry Fineberg, formerly head of the psychiatric department at Children's Memorial Hospital, who in January, 1958, consented to serve as acting director of the mental health unit until a full-time director was named.

Dr. Strauss Honored.—Dr. Sidney Strauss was honored by the Chicago Heart Association, which he helped found in 1922, at an open house celebration held at the association's new headquarters at 22 W. Madison on Sept. 24. Dr. Strauss, 81, is senior attending physician at the Michael Reese Hospital whose staff he joined in 1911. Dr. Strauss was among a small group of physicians who established what was originally called the Association for the Prevention and Relief of Heart Disease, later changed to the Chicago Heart Association in 1925. In 1924 he helped organize the American Heart Association and was a member of the first board of directors. The Sidney Strauss Conference Room was dedicated to him at the new headquarters Sept. 24.

Professor Knaus to Lecture.—Prof. Hermann H. Knaus, director, department of gynecology and obstetrics, Hospital of Vienna–Lainz, Austria, will present a lecture, "Post-Maturity, Determination and Treatment," Nov. 19, 4:30 p. m., in Dora DeLee Hall, The Chicago Lying-in Hospital, of the University of Chicago School of Medicine.

MARYLAND

New General Hospital in Baltimore.—The new Sinai Hospital, reportedly the only general hospital in the northwest section of Baltimore, was dedicated Sept. 20 and will be officially opened in November. The hospital, built at a cost of over 20 million dollars, has a total of 483 beds, 171 more than there are at the old Sinai on Monument Street. It is composed of nine units, including the Mount Pleasant Building completed in 1953, covers 600,991 square feet of space, has parking facilities for over 800 cars, a heliport, and overnight accommodations for relatives for very ill patients. Besides the Mount Pleasant Building, other units are the General Hospital Building, Louis and Henrietta Blaustein Obstetric and Gynecology Building, Morris Schapiro and Family Research Building, Hecht School of Nursing, Hofberger Nurses Residence, Rosenbloom Staff Residence, Zamoiski Auditorium, and Bettie S. Fuechsl and Ferdinand and Henrietta Fuechsl Service and Utility Buildings, all connected by underground corridors. Except in the pediatric department, there are no more than two beds in any room, even in the wards. Patient rooms are provided with individual control for air-conditioning, have piped-in oxygen and suction, and private lavatories. There are 40 beds to each nursing station, and each 40-bed unit has its own solarium. For very ill patients there will be two intensive nursing units of four beds each. Ten operating rooms radiate from a central sterile and scrub-up area. The buildings have been so constructed that additional floors and wings can be added. There are 40 acres of land available for future expansion. The Aaron and Lillie Straus Out-Patient Department can handle 100,000 patient visits a year, and the Kann Memorial Emergency Service is equipped to handle several hundred patients a day. The new hospital is located on 50 acres of land. It is contemporary in design, built of red brick with white Vermont marble used for outside trim and Israeli marble used in the lobby of the

The new Sinai Hospital, Baltimore.

General Hospital Building. The hospital, a constituent agency of the Associated Jewish Charities, is nonsectarian.

MASSACHUSETTS

Dr. Gross Receives Heart Award.—The 1959 Albert Lasker Award of the American Heart Association was presented Oct. 24 to Dr. Robert E. Gross, Boston. The award, given annually "for distinguished achievement in the field of cardiovascular research," was conferred during the association's annual scientific sessions. Dr. Gross, the first surgeon to be thus honored, is Ladd Professor of Children's Surgery at Harvard Medical School and surgeon-in-chief at Boston's Children's Hospital. He is a founder and a member of the board of directors and executive committee of the American Heart Association. The Lasker award for cardiovascular research was established in 1953 by the Albert and Mary Lasker Foundation in cooperation with the American Heart Association. Previous winners include Dr. Paul Dudley White, Boston; Dr. Albert Szent-Gyorgyi, Woods Hole, Mass.; Dr. Carl J. Wiggers, Cleveland Heights, Ohio; Dr. Louis N. Katz, Chicago; Dr. Isaac Starr, Philadelphia; and Dr. Irvine H. Page, Cleveland.

MICHIGAN

Dr. Gray Honored.—Dr. Jacques Pierce Gray, Detroit, visiting lecturer of the American Medical Writers' Association, was recipient of the Distinguished Service Award of the association for 1959. The award is given annually to a fellow of the asso-

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ciation "who has made distinguished contributions to medical literature or rendered unusual and distinguished services to the medical profession."

Dr. Walker to Give Annual Lecture.—Dr. A. Earl Walker, Baltimore, professor of neurosurgery and chairman of the department of neurological surgery at Johns Hopkins Hospital, will present the annual Alpha Omega Alpha Lecture at Wayne State University College of Medicine, Detroit, Nov. 20, 11 a. m. to 12 noon in the Wayne County Medical Society Auditorium. The subject he has chosen is titled "A Modern View of the Falling Sickness."

Emeritus Professors Receive Honorary Degrees.—Honorary doctor of law degrees were presented at the annual University of Michigan Medical Honors Convocation Oct. 17 to Drs. Frederick A. Coller and Udo J. Wile, emeritus professors of the University of Michigan Medical School, Ann Arbor. The convocation closed the three-day meeting of the seventh Triennial Medical Alumni Conference. Dr. Coller, major speaker at the convocation, retired in 1957 after serving as head of the surgery department for 27 years. The Frederick A. Coller Society, founded in 1947, is made up of surgeons who trained under him. He is one of 50 members of the Royal College of Surgeons in England. Dr. Wile, professor emeritus of dermatology and syphilology and chairman of the department for 35 years, was cited for his "contributions to the scientific knowledge of diseases and his advances in medical theory and practice." Dr. Wile reportedly established the first university hospital clinic in the United States for training dermatologists and syphilologists.

MINNESOTA

British Lecturer.—Dr. James Purdon Martin, emeritus chief of staff in the National Hospital for Neurologic Diseases and Epilepsy, Queen's Square, London, England, gave a lecture, "Extrapyramidal Dyskinesias," at the Mayo Foundation, Rochester, Sept. 29.

Dr. Buie Named Royal Society Member.—Dr. Louis A. Buie Sr., Rochester, founder of the section of proctology of the Mayo Clinic and a member of the staff from 1919 until his retirement in 1955, was made an honorary member of the Royal Society of Medicine of England on July 1. The certificate of honorary members, signed by Dr. Henry R. Thompson, London, president of the society, indicates that the honor was conferred on Dr. Buie "for distinguished services to science."

MISSOURI

Foreign Lecturer.—Dr. S. C. Sen, radiologist of New Delhi, India, lectured Oct. 9 in the University of Missouri Medical Center Auditorium. His subject was "Brief Glimpses into Ancient Indian Medicine and Traditional Chinese Medicine." Since 1947 Dr. Sen has been a member of the Council of the World Medical Association and was its secretary for Asia for nine years.

NEW YORK

Dr. Yanover Cited.—On Sept. 3 Dr. Robert R. Yanover, Flushing, chairman of the medical advisory board of Abilities Inc., Albertson, was given a presidential citation, "for his contribution to the advancement of the disabled." Abilities Inc., with which Dr. Yanover has been associated since its founding seven years ago, is an electronics manufacturing firm employing only disabled persons.

Alumni Honor Dr. McCann.—Dr. William S. McCann, Rochester, was presented the annual Gold Medal Award at the 15th annual meeting of the University of Rochester Medical Alumni Association, Oct. 10. Dr. McCann, who retired on June 30, 1957, as chairman of the department of medicine, a position he had held since the School of Medicine and Dentistry was opened in 1925, is now emeritus professor of medicine.

Radio Medical Conferences.—Albany Medical College inaugurated its fifth season of two-way radio medical conferences Oct. 6, Dr. Frank M. Woolsey Jr., Albany, associate dean and director of postgraduate education, announced. The conferences are broadcast to doctors at 24 hospitals in New York, Massachusetts, and New Hampshire. The current season will extend through April, 1960, with conferences scheduled on a three-times-a-week basis. The hour-long conferences cover a variety of medical and surgical topics. Last year, more than 700 individual physicians took part in one or more conferences. The total attendance for the year was 5,425. Albany Medical College broadcasted its initial conference in December, 1955. E. R. Squibb & Sons, pharmaceutical division of the Olin Mathieson Chemical Corporation helps support the conferences by a grant-in-aid. Faculty members from six eastern medical schools participate.

New York City

Biologist to Give Annual Lecture.—The fifth annual Israel S. Wechsler Lecture will be given Dec. 11, 8:30 p. m., in the Blumenthal Auditorium of the Mount Sinai Hospital. Paul A. Weiss, Ph.D., head, department of developmental biology, Rockefeller Institute, will present "Problems of Specificity in the Development and Functioning of the Nervous System."

Hospital Panel on Medical Genetics.—The Adelphi Hospital medical staff will present a panel meeting on medical genetics, Wednesday, Nov. 25, at the new auditorium. Dr. Alexander S. Wiener, Brooklyn, will moderate the panel and present "Heredi-

tary Disorders of the Blood." Dr. Victor A. McKusick, Baltimore, will give "Hereditary Disorders of Connective Tissue" and Dr. Franz J. Kallmann, will present "Hereditary Disorders of the Nervous System." For information, write the Adelphi Hospital, 50 Greene Ave., Brooklyn 38.

Annual Lecture on Skin Diseases.—The department of dermatology and syphilology of the New York University Post-Graduate Medical School announced the ninth annual Sigmund Pollitzer Lecture to be given by Prof. Harold F. Blum Nov. 17, 8 p. m., in Classroom B of Alumni Hall, 550 First Ave. Professor Blum, physiologist at the National Cancer Institute and visiting professor at Princeton University, will present "Carcinogenesis by Ultraviolet Light: Experiment and Interpretation." The Pollitzer Lectures are made possible by a grant from Mrs. Sigmund Pollitzer, who established the lectureship in honor of her husband, the late Dr. Sigmund Pollitzer, former professor of dermatology and syphilology at the Post-Graduate Medical School. Under the terms of the grant, "outstanding" scientists and teachers are invited to speak in selected subjects relating to skin diseases.

Grants for Research.—On the recommendation of the Health Research Council, the New York City Board of Estimate on Oct. 8 approved 14 medical research grants which will total $1,023,309 over a five-year period. Under the terms of the grants, $270,713 will be spent in the first year, the remaining $752,596 in the following four years. Grants were made to medical schools in New York City for research work on specific projects to be conducted in five municipal hospitals. In addition, newly created "New York City Investigatorships" were awarded to six young university scientists who will do research work in municipal hospitals. The grants to the medical schools will support both laboratory and clinical research in cancer, infectious diseases, narcotic addiction, disorders of metabolism, and diseases of the cardiovascular system, central nervous system, and pulmonary system. The Health Research Council was set up by Mayor Wagner in September, 1958, "to work out policy and guide the City in allocating city funds which will enable scientists to carry on research work in health and medical problems." Dr. Walsh McDermott, Livingston Farrand Professor of Public Health and Preventive Medicine at Cornell University Medical College, is chairman of the council. The grants voted by the Board of Estimate are the first to be made under the program.

OHIO

Fellowships in Industrial Medicine.—The University of Cincinnati's Institute of Industrial Health is offering graduate fellowships in industrial medicine. The institute, in the College of Medicine, provides professional training for graduates of approved medical schools who have completed at least one year of internship. The three-year program leading to the degree of doctor of industrial medicine satisfies the requirements for certification in occupational medicine by the American Board of Preventive Medicine. Two years are devoted to intensive academic and clinical study in industrial medicine. A third year is spent in residency in an industrial medical department or in some comparable organization. Stipends for the first two years are from $3,000 to $4,000, depending upon marital status. In the final or residency year the fellow is compensated by the organization in which he is completing his training. Two other programs are offered to qualified applicants: a one-year course, to applicants who wish to become candidates for the degree of master of science; and a three-year academic program leading to the degree of doctor of science, to those who wish to pursue careers in teaching and research. Fellowship stipends are available in these programs. For information, write: Secretary, Institute of Industrial Health, College of Medicine, Eden and Bethesda Avenues, Cincinnati 19.

OKLAHOMA

Dr. Donahue Resigns as Mental Health Director.—Dr. Hayden H. Donahue, Oklahoma City, director of the Oklahoma Department of Mental Health for the past seven years, announced his resignation on Aug. 4, "to seek a residency in psychiatry, do mental health research, and complete the writing of a book." It has been reported that Dr. Donahue has accepted the position of assistant director, Arkansas State Hospital, Little Rock. Governor J. Howard Edmondson issued a proclamation stating: "Primarily under the director of Dr. Hayden H. Donahue, Oklahoma Mental hospitals and schools for the retarded have risen . . . to a position reflecting dignity, pride and national pre-eminence." The proclamation declared Sept. 22 as Donahue Appreciation Day and a testimonial dinner was held on that date with Governor Edmondson as the principal speaker and Dr. George H. Guthrey, Oklahoma City, as master of ceremonies.

PENNSYLVANIA

Philadelphia

Dinner for Hospital Alumni.—The 73rd annual dinner of the Association of Ex-Residents and Resident Physicians of the Philadelphia General Hospital will be held on Tuesday, Dec. 1, at 7 p. m., at Williamson's Presidential Dining Rooms, Presidential Apartments, City Line and Schuylkill Expressway, Philadelphia. All members are urged to attend. For information, write Dr. William W. Wilson, Secretary-Treasurer, 133 S. 36th St., Philadelphia 4.

University News.—The University of Pennsylvania held a special convocation to commemorate the 75th anniversary of the founding of the School of Veterinary Medicine Oct. 3. The convocation was sched-

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uled to coincide with the 77th annual convention of the Pennsylvania State Veterinary Medical Association.—A group of 37 Italian physicians were guests of the Temple University Medical Center Aug. 23. The doctors, all professors of medical schools in Italy, toured medical centers in the United States and Canada.

Dr. Nichols Appointed Department Head.—The appointment of Dr. Henry T. Nichols as professor and head of the department of thoracic surgery was confirmed by the board of trustees of Hahnemann Medical College and Hospital. Dr. Nichols had been acting head of the department since September, 1958. A member of the American Board of Surgery and the Board of Thoracic Surgery, Dr. Nichols is affiliated with the Veterans' Administration Hospital, Rolling Hill Hospital (Jenkintown), Albert Einstein Medical Center and Womans' Hospital.

Research Laboratory Dedicated.—On Sunday, Sept. 20, a new research laboratory of Wills Eye Hospital, headed by Dr. Irving H. Leopold, was dedicated. The principal address will be delivered by Governor David L. Lawrence of the Commonwealth of Pennsylvania. The research department of the Wills Eye Hospital was formally initiated in 1950. Through a Ford Foundation contribution and matching National Institutes of Health funds and other contributions, the new laboratory building was made possible. There are 26 full-time research workers, in addition to members of the hospital staff who engage in part-time research. The new building is equipped with departments of pathology, microbiology, biochemistry, pharmacology, and radioactive isotopes. The laboratory is an unendowed department that must depend on new grants and the support of friends for its maintenance.

RHODE ISLAND

Medical History Meeting.—The Benjamin Waterhouse Medical History Society will meet in combination with the Providence Medical History Society at the Rhode Island Hospital Monday, Nov. 16. Dr. Charles W. Robertson, associate professor of surgery, Boston University School of Medicine, will be speaker, presenting "Some Observations on Presidential Illnesses." For information, write Dr. John J. Byrne, 818 Harrison Ave., Boston 18, Secretary (KE 6-8600).

VERMONT

Dedicate New Medical Building.—A program of dedication for the new medical building at the University of Vermont College of Medicine, Burlington, was held Sept. 24-26 in celebration of completion of the first phase of the proposed building program. The new building, the first to be built in nearly 55 years, provides new and expanded research facilities. The first medical building for the college, Pomeroy Hall, dedicated in 1829, is still used by the university for offices and classrooms. A symposium, "Peptic Ulcer," Sept. 24, was opened by Dr. George A. Wolf Jr., dean of the college of medicine. On Sept. 25, medical grand rounds were held and the first annual Beaumont Lecture, "Gastric Research in the Hundred Years Since Beaumont," was given by Dr. Stewart Wolf, professor of medicine, University of Oklahoma, Oklahoma City. At the dedication ceremonies, Sept. 16, Dr. Ernest M. Allen, chief, division of research grants, National Institutes of Health, United States Public Health Service, presented an address.

WASHINGTON

State Medical Election.—The Washington State Medical Association elected the following 1959-1960 officers: president, Dr. Frederick A. Tucker, Seattle; president-elect, Dr. Homer W. Humiston, Tacoma; immediate past-president, Dr. Emmett L. Calhoun, Aberdeen; vice-president, Dr. Edward C. Guyer, Seattle; secretary-treasurer, Dr. Wilbur E. Watson, Seattle; and speaker, House of Delegates, Dr. Dean K. Crystal, Seattle. The executive secretary is Mr. Ralph W. Neill, 1309 Seventh Ave., Seattle 1.

WISCONSIN

Rehabilitation Center Opens.—The University of Wisconsin Medical Center's Respiratory and Rehabilitation Center, aimed at "restoration of disabled patients to the greatest possible physical, mental, social, and vocational capacity," began serving the state Sept. 11. The center is located in the remodeled seventh floor of University Hospitals, Madison, where opening of the new facility was observed at brief ceremonies the afternoon of Sept. 11. A Wisconsin physician may refer to the center any patient with a severely disabling disease or injury which demands long-term reorganization of the patient's life. Dr. Arthur Siebens, director, and Dr. W. Theodore Bruns, assistant director, will be responsible for treating the medical problems and guiding the staff teamwork. The center has an orthotist to design, adapt, and make devices for the patient. Aid from the university department of clinical psychology and the Speech and Hearing Clinic will be available. The facility is also concerned with basic research and studies relating to the mechanics and measurement of breathing. The third major purpose of the center is teaching. Several staff members are on the Medical School faculty and will teach in their respective fields. The new facility is supported by funds from the State of Wisconsin and organizations such as the National Foundation, the Sister Elizabeth Kenny Foundation, the Benjamin Wishner Estate, the Bess Heath Estate, the United Fund of Marathon County, and the Oscar Mayer Foundation of Madison.

GENERAL

Dr. Wilson Becomes Tuberculosis Director.—Dr. Julius L. Wilson became full-time director of medical education for the National Tuberculosis Association and its medical section, the American Trudeau Society, as of Oct. 1. For the past six years Dr. Wilson has been serving as part-time director of medical education while serving also as director of the Henry Phipps Institute for the Study and Prevention of Tuberculosis of the University of Pennsylvania, Philadelphia.

Meeting on Cerebral Palsy in Los Angeles.—The American Academy for Cerebral Palsy will meet at the Statler-Hilton Hotel, Nov. 30-Dec. 2. Instructional courses and question-and-answer luncheons will be held Nov. 30 and Dec. 1. Dr. Alvin J. Ingram, Memphis, Tenn., will give the presidential address the morning of Dec. 1. A research afternoon is planned for Dec. 1, with seven papers scheduled, including discussion periods. Round-table discussions will be conducted the morning of Dec. 2. Scientific exhibits are planned.

Western Surgical Meeting.—The 67th annual meeting of the Western Surgical Association will be held Nov. 19-21 at the Broadmoor Hotel, Colorado Springs, Colo. A total of 36 papers is scheduled to be presented at the four scientific sessions. Dr. James T. Priestley, Rochester, Minn., will present "Surgery, Science, and Education" as the president's address the morning of Nov. 20. The annual banquet is planned for the evening of Nov. 20. A ladies' program is arranged. For information, write Dr. John T. Reynolds, 612 N. Michigan Blvd., Chicago 11, Secretary.

Meeting on Psychoanalysis.—The scientific sessions of the midwinter meeting of the Academy of Psychoanalysis will be held Dec. 5-6, 9 a. m. to 5 p. m., at the Hotel Roosevelt, New York City. The theme of the first day's meeting will be "Psychoanalytic Concepts in Allied Fields." Harold Lasswell, Ph.D., will speak on the implications psychoanalytic concepts have for political science; Weston LeBarre, Ph.D., on the implications for anthropology; and Talcott Parsons, Ph.D., on the implications for social science. The second day's meeting will be devoted to a series of clinical papers by members of the academy. The address of the academy is 125 E. 65th St., New York 21.

Propose Health and Research Year.—The governments of the American Republics, plus those of France, The Netherlands, and the United Kingdom went on record as supporting the establishment of an International Health and Medical Research Year. The action came during a session of the 11th annual meeting of the Pan American Health Organization's directing council. Meeting also as the regional committee for the Western Hemisphere of the World Health Organization, the council's vote goes to WHO Director-General M. G. Candau in Geneva. U. S. Surgeon General Dr. Leroy E. Burney presented the resolution favoring the year on behalf of his delegation.

Conference on Electrical Techniques in Medicine.—The 12th annual Conference of Electrical Techniques in Medicine and Biology will be held Nov. 9-12 at the Hotel Sheraton, Philadelphia. Besides two general sessions, special sessions are arranged under the following titles:

Ultraviolet Radiation
Cardiovascular
Microwave Radiation
Ultrasonic Radiation
Infrared Radiation

An exhibition and demonstration of electrical medical equipment and accessories is planned. More than 40 papers will be presented at the special sessions, and more than 20 additional papers will be concerned with cardiovascular techniques and instrument advances in biomedical electronics. Chairman of the conference committee is Herman P. Schwan, Ph.D., Philadalephia. Advanced registration is $5. A program of tours is planned.

List of Western Meetings.—Starting in November, the *Rocky Mountain Medical Journal* will publish monthly a bulletin entitled "What goes on." Physicians in the following states will receive the publication: Alaska, Arizona, Colorado, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, and Wyoming. The medical societies in these states are cooperating in the project. "What goes on" will list medical meetings and special lectures of interest in an effort to keep physicians informed of area postgraduate education opportunities. It will also include notification regarding postgraduate sessions offered by medical schools as well as speakers sponsored by hospitals, specialized medical organizations, and area medical societies. Listings will be grouped by geographical divisions for the month covered by the particular issue. A separate section will carry future dates. "What goes on" is sponsored by Lederle Laboratories, a division of the American Cyanamid Company, and is being sent free to all physicians in the 11-state region.

Travel Grants for Congress of Endocrinology.—The first International Congress of Endocrinology will be held in Copenhagen, Denmark, July 18-23, 1960. The Endocrine Society has obtained funds to provide a limited number of allotments in support of travel to the congress for scientists residing in the United States and Canada who may require such assistance. Individual allotments will not exceed $750 each. Application for travel allotment should be submitted in duplicate in the form of a letter

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giving information on age, training, publications, academic or professional title, and society affiliation. Applicants who plan to submit papers for presentation at the congress should include the proposed title of each paper. Such letters should be submitted before Nov. 15 and should be addressed to Dr. Henry H. Turner, Secretary, The Endocrine Society, 1200 North Walker, Oklahoma City 3, Okla. Applicants will be responsible for their own passports, registration, travel arrangements, and hotel reservations. For information on registration and submission of papers, write The Secretariat, Hormonafdelingen, Statens Seruminstitut, Copenhagen.

Meeting of Northwest Physicians.—The American College of Physicians Pacific Northwest Region meeting for Oregon, Washington, and British Columbia will be held Nov. 20-21 at the Sheraton Hotel, Portland, Ore. Of the papers scheduled for presentation, the following include invited authors:

Congestive Failure Due to Auricular Fibrillation: A Twenty-Five-Year Follow-up, Dr. Isidor C. Brill, and Dr. Edward E. Rosenbaum, Portland.

Mortality in Myocardial Infarction in the Older Age Group, Dr. Llewellyn N. Roberts, Victoria, B. C.

Auscultatory Implications of the Split Second Heart Tone, Dr. Charles P. Wilson, and Dr. Marvin J. Weinstein, Rochester, Minn.

Evaluation of Pulmonary Function, Dr. Donald M. Pitcairn, Portland.

The Incidence of Obstructive Pulmonary Disease in Chronic and Custodial Tubercular Patients, Dr. Carroll J. Martin, and Dr. Wilbur Hallett, Seattle.

Malabsorption in Gastrocolic Fistula, Dr. John A. Benson Jr., Boston.

Newer Tests for Diagnosis of Acquired Hemolytic Anemia, Dr. Bernard Pirofsky, Portland.

At the dinner the evening of Nov. 20, Dr. Howard P. Lewis, Portland, president of the college, will present an address. For information, write the American College of Physicians, 4200 Pine St., Philadelphia 4.

Psoriasis Research Award.—The department of dermatology, Baylor University College of Medicine, Houston, Texas, announced the Mr. and Mrs. J. M. Taub International Memorial Award for Psoriasis Research. This annual award of $1,000 was established in 1957, by Carol and Henry J. N. Taub in honor of their grandparents, Mr. and Mrs. Henry J. N. Taub. The award is designated for the individual or group who has done the "most outstanding investigative work" in this field. Results of the research must have been presented before a dermatological medical society or published in one of the recognized medical journals during the calendar year. The name of any applicant for the award, together with supporting data, should be submitted for consideration by Dec. 31 of the same year. The recipient will be determined by a committee composed of Drs. Marcus R. Caro, Chicago; Edward P. Cawley, Charlottesville, Va.; Arthur C. Curtis, Ann Arbor, Mich.; Eugene M. Faber, San Francisco; John M. Knox, Houston, Texas; Aaron B. Lerner, New Haven; and Carl T. Nelson, New York City. If in the opinion of the committee a given calendar year fails to yield a deserving contribution, the award will not be given. Address all communications to Dr. John M. Knox, Department of Dermatology, Baylor University College of Medicine, Houston 25, Texas.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

Area	Oct. 10, 1959 Paralytic Type	Oct. 10, 1959 Total Cases	Oct. 11, 1958 Total
New England States			
Maine	14	14	..
New Hampshire	..	..	..
Vermont	..	..	..
Massachusetts	4	7	2
Rhode Island	..	..	..
Connecticut	3	3	3
Middle Atlantic States			
New York	15	20	16
New Jersey	7	8	17
Pennsylvania	2	2	7
East North Central States			
Ohio	6	12	19
Indiana	3	6	9
Illinois	9	19	10
Michigan	6	14	98
Wisconsin	1	2	3
West North Central States			
Minnesota	14	15	4
Iowa	9	16	..
Missouri	9	14	15
North Dakota	..	..	3
South Dakota	..	..	..
Nebraska	2	7	3
Kansas	3	3	3
South Atlantic States			
Delaware	..	..	1
Maryland	4	4	1
District of Columbia	..	..	..
Virginia	10	10	12
West Virginia	12	12	17
North Carolina	16	16	..
South Carolina	3	3	1
Georgia	3	3	3
Florida	2	3	12
East South Central States			
Kentucky	4	6	4
Tennessee	11	14	8
Alabama	4	4	1
Mississippi	1	1	3
West South Central States			
Arkansas	8	21	..
Louisiana	..	4	4
Oklahoma	1	2	..
Texas	10	16	16
Mountain States			
Montana	..	..	1
Idaho	..	1	..
Wyoming	..	..	1
Colorado	1	2	1
New Mexico	..	..	1
Arizona	3	3	2
Utah	..	..	..
Nevada	..	..	..
Pacific States			
Washington	7	7	9
Oregon	6	8	..
California	12	13	9
Alaska	4	5	..
Hawaii	..	..	2
Territories and Possessions			
Puerto Rico	..	..	..
Total	229	329	321

Report on Married Couples.—The Metropolitan Life Insurance Company reported that currently the United States has about 39½ million married couples. In almost one-half of them the husband is 25 to 44 years old. According to the Bureau of Census, the total number of married couples increased

by 10⅔ million from 1940 to 1958. Nearly the same growth is expected in the like period ahead, with a total of about 50⅓ million married couples by 1975. The rising tide of young people and the high marriage rates of the postwar years have produced an increase of about 50% from 1940 to 1958 in the number of couples with husbands under 25 years of age. The reported outlook is that the number of such young couples will more than double from 1958 to 1975, reaching a total of about 4.7 million. The number of couples with husbands at age 65 or older mounted by 73% from 1940 to 1958, with a further increase of 36% expected by 1975. This growth reportedly reflects the aging of the population. For couples in which the husband is 25-44 years of age, the increase between 1940 and 1958 averaged about 30%. Couples headed by husbands in midlife have been increasing and are expected to continue to do so.

Smallpox Declining in the Americas.—Smallpox cases reported in the Americas dropped fourfold during the past decade, according to a report presented before the directing council of the Pan-American Health Organization. While 18,352 cases were reported in the Americas during 1949, only 4,311 were reported last year. Yet smallpox is still a major public health problem in the hemisphere, says the report. During this 10-year period, of the total of 103,491 cases reported in 15 countries and other areas, there were at least 16,000 deaths. The directing council urged all countries of the Americas to ". . . accord the smallpox eradication program the importance and priority it deserves, from the viewpoint of both national and international health." The 15th Pan American Sanitary Conference, held last year in San Juan, Puerto Rico, declared smallpox a health problem requiring the attention of all countries and requested that necessary measures be taken for the eradication of the disease from the hemisphere. Since 1948 PASB has spent about $350,000 in aiding the governments of the hemisphere in combatting smallpox. The 90 member States of the World Health Organization, meeting during the 12th World Health Assembly in Geneva, voted to make the smallpox eradication campaign global earlier this year.

National Index on Deafness, Speech, and Hearing—Gallaudet College, Washington, D. C., and the American Speech and Hearing Association established a National Index on Deafness, Speech, and Hearing. This index will combine the present indexing and abstracting functions of the Central Index of Research on the Deaf at Gallaudet College and the projected indexing and abstracting functions of the American Speech and Hearing Association. The general policies of the national index will be formulated by a committee composed of representatives of Gallaudet College and representatives of the Association. The index, to be located at Gallaudet College, will be directed by Stephen P. Quigley, Ph.D., Washington, D. C. The purpose of the index is "to index and abstract all professional literature pertaining to deafness, speech and hearing and to make this material readily available to all interested persons." Present and future literature will be included as will the relevant past literature. The index will make the collected material available through a regular, professional publication. The National Index on Deafness, Speech and Hearing is made possible in part by a grant from the Office of Vocational Rehabilitation of the Department of Health, Education, and Welfare. For information, write Stephen P. Quigley, Ph.D., Director, National Index on Deafness, Speech and Hearing, Gallaudet College, Washington 2, D. C.

Fellowships for Residents in Pediatrics.—The American Academy of Pediatrics will grant 28 or more fellowships to pediatric residents for the year beginning July 1, 1960, and covering a period of six months to one year. These fellowships, created to enable young physicians, who are legal residents of the United States or Canada and who are in financial need, to complete their pediatric training, have been provided in two groups. Mead Johnson & Company, has made possible the awarding of 18 or more fellowships to carry a stipend of from $500 to $1,000 each, depending on the need and the length of time required to complete training. A second group of 10 fellowships, each carrying a stipend of $500 and awarded on the same basis as the others, has been made available through a grant to the academy from the Gerber Baby Food Foundation. Requirements for the awards are (1) a letter from the chief of service indicating that the individual will have completed by July 1, 1960, one year of pediatric training credited by the American Board of Pediatrics; that the resident has performed his work ably; and that there is need for financial assistance; (2) a letter from the resident requesting the fellowship stating that he intends to enter pediatric private practice at the conclusion of his residency training. Those interested in applying may correspond with the American Academy of Pediatrics, 1801 Hinman Ave., Evanston, Ill. The deadline for the receipt of applications will be Feb. 15.

Fund to Aid Interns and Residents.—A $400,000 George W. Merck Memorial Loan Fund has been established by the Merck Company Foundation "to help meet an important need for financial aid to interns and residents." The fund will assist "deserving interns and residents to seek the best possible postgraduate training in teaching hospitals before entering practice." It is estimated that 60 to 100 young doctors will benefit each year from the fund. The 18 medical schools participating are associated

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with the following universities: Boston, California, Chicago, Columbia, Cornell, Harvard, Illinois, Johns Hopkins, New York, Northwestern, Pennsylvania, St. Louis, Tufts, Vanderbilt, Vermont, Virginia, Washington (St. Louis), and Yale. They were selected on the basis of close personal friendships which the late George W. Merck had with members of their faculties or staffs. Graduates of other medical schools also may be eligible for loans if they take the internship or residency at any of the 48 teaching hospitals affiliated with the participating schools. Administration of the fund will be by the deans of the medical schools. The Merck Company Foundation will allocate the $400,000 over a period of eight years, by which time the fund is expected to be self-sustaining. Initial payments to the 18 schools have been completed, so that funds will be available in 1959. The Merck Company Foundation is a nonprofit corporation supported by Merck & Co., Inc. It makes contributions to education and other causes.

Society News.—The **American Congress of Physical Medicine and Rehabilitation** elected the following officers for 1959-1960: Dr. Frederic J. Kottke, Minneapolis, president; Dr. Donald A. Covalt, New York City, president-elect; Dr. Donald J. Erickson, Rochester, Minn., first vice-president; Dr. Jerome S. Tobis, New York City, second vice-president; Dr. Louis B. Newman, Chicago, third vice-president; Dr. Charles D. Shields, Washington, D. C., fourth vice-president; Dr. William J. Erdman, II, Philadelphia, fifth vice-president; Dr. Frances Baker, San Mateo, Calif., secretary; Dr. Frank H. Krusen, Rochester, Minn., treasurer; Dr. Walter J. Zeitel, Cleveland, executive director; and Dr. Glenn Gullickson Jr., Minneapolis, assistant to the executive director. Miss Dorothea C. Augustin, Chicago, is executive secretary.——For the year Sept. 12, 1959, to Sept. 10, 1960, the following are the officers of the **American Association of Obstetricians and Gynecologists:** president, Dr. Robert A. Ross, Chapel Hill, N. C.; president-elect, Dr. John L. Parks, Washington, D. C.; vice-president, Dr. Emmett D. Colvin, Atlanta, Ga.; secretary, Dr. Clyde L. Randall, Buffalo; assistant secretary, Dr. Clayton T. Beecham, Philadelphia; and treasurer, Dr. Harold L. Gainey, Kansas City, Mo.——At the annual meeting of the **American Association of Medical Clinics** the following were elected: Dr. Russel V. A. Lee, Palo Alto, Calif., president; Dr. Harold D. Caylor, Bluffton, Ind., first vice-president and president-elect; Dr. Bernard A. Watson, Clifton Springs, N. Y., second vice-president; and Dr. Joseph B. Davis, Davis Clinic, 131 N. Washington St., Marion Ind., secretary-treasurer.

Survey of Surgery.—The Metropolitan Life Insurance Company reported that well over 10 million surgical operations are performed in this country each year, according to the National Health Survey program of the U. S. Public Health Service. No less than 60% of all patients in short-stay hospitals receive surgical treatment. The scope of surgery has broadened, especially in the last two decades, and the risk of operation has lessened. In a review of the experience of one large hospital, covering more than 100,000 operations and anesthetic procedures of all types during 1945-1954, the surgical mortality was 43% below that of 1925-1934. Reductions in the mortality associated with a number of specific operations were reported in a St. Louis study. There was a decline of 88% between the two periods 1916-1938 and 1948-1952 in the surgical mortality of one type of operation for gallbladder disease. About as rapid was the decline from 1920 to 1953 for thyroid operations in cases of toxic goiter. Within a period of 15 years, a drop of nearly 85% was reported for closure of perforated peptic ulcers. Other operations with reductions in surgical risk in this St. Louis study were corrections of obstructions of the small intestine, partial gastric resection in duodenal ulcer, esophagectomy in cancer, and radical mastectomy. Advances in cardiac surgery were illustrated by a study of several Boston hospitals with patients having a mitral valvuloplasty. Among patients with some impairment of function or with progressive symptoms due to the disease, the rate of 14% in 1949-1951 was cut to 4% in 1951-1953. Subsequently the surgical mortality dropped to less than 1% for the patients in the study who had the operation in 1953-1956.

Report on Medical Manpower.—The ratio of physicians to population in the United States, which has ranged between 131 and 135 per 100,000 persons for 20 years, "will drop to 126 per 100,000 by 1975 unless the rate of graduating students increases substantially," a report issued by the Public Health Service indicates. The number of dentists per 100,000 persons in the population will decline even more sharply, the report states. Entitled "Health Manpower Source Book, Section 9: Physicians, Dentists, Nurses," the report reveals trends in the education, location, and specialization of these professional personnel. In the academic year 1958-1959, the 85 medical schools in the United States graduated 6,895 physicians. To maintain the present physician-population ratio, U. S. medical schools reportedly would need to graduate about 10,360 students by 1975—nearly 3,000 above the 7,410 graduates currently predicted for that year. The 47 dental schools in the United States graduated 3,083 dentists in the academic year 1957-1958. Despite the addition of eight new dental schools since World War II and large increases in the number of graduates, the ratio of dentists to population remains below pre-World War II levels. According to the report, the ratio of dentists was 62 per 100,000 in 1940, 57 in 1958, and is expected to decline to about 50 per

100,000 in 1975. There should, however, be an increase in the ratio of professional nurses—from 268 per 100,000 population in 1958 to 284 per 100,000 in 1970, the report indicates. The nurse-population ratio has increased almost fivefold in the United States since 1910. In the academic year 1957-1958, the 1,145 schools of nursing in the United States enrolled about 113,000 students and graduated 30,410 nurses. The report also contains information about doctors of osteopathy. The current combined ratio of doctors of medicine and osteopathy to population is about 140 per 100,000 persons and "this is expected to decline to 133 per 100,000 by 1975." The report, listed as Public Health Service Publication No. 263, Section 9, may be purchased from the Superintendent of Documents, Government Printing Office, Washington 25, D. C., at 50 cents per copy. Single free copies may be obtained from the Division of Public Health Methods, Public Health Service, Washington 25, D. C.

CANADA

Dr. McRae Receives Radiology Medal.—Dr. Donald L. McRae, Montreal, associate professor of radiology, McGill University, received the Caldwell Lecture Medal of the American Roentgen Ray Society following presentation of the Caldwell Lecture during the 60th annual meeting of the society. The title of Dr. McRae's address was "The Significance of Abnormalities of the Cervical Spine." The Caldwell Lecture honors the late Dr. Eugen W. Caldwell, pioneer user of radiation in medicine. Dr. McRae is the first Canadian to present the Caldwell Lecture.

FOREIGN

Congress on Audiology in Bonn.—The fifth congress of the International Society of Audiology will be held Sept. 28-Oct. 1, 1960, at Bonn, German Federal Republic. Three round-table discussions are arranged: the cortical auditory function and its disturbances in adults and in children; physiology, functional pathology, and clinical significance of recruitment; and adaptation and related phenomena —their clinical significance. Free communications are planned. The official languages will be German, French, English, and Spanish with simultaneous translation. For information, write the General Secretary, International Society of Audiology, 4, Rue Montvert, Lyon, France.

Civil Defense Conference Postponed.—The fourth International Civil Defense Conference, which was to be held in Paris Sept. 28-Oct. 3, as well as the first International Exhibition of Civil Defense Equipment, have been postponed. During discussions in Paris, "objections were raised regarding some of the items on the agenda, i. e., the functioning of the World Radioactivity Warning Centre, set up in Geneva in November, 1958." Since the preparatory work for the fourth International Civil Defense Conference had been completed at the time of its cancellation, the executive bureau is taking steps to organize the conference and exhibition at a date and in a place which will be fixed subsequently and will be chosen to suit the participants already registered.

Congress on Medical Photography.—The medical section of the Deutsche Gesellschaft für Photographie eV. (DGPh), Cologne, Germany, announced that, contrary to previous information, the first International Congress on Medical Photography and Cinematography will take place Sept. 27-30, 1960, in connection with the "photokina" (Sept. 24-Oct. 2) at Cologne. Purpose of the congress will be to show the present status of photographic and cinematographic exposure and reproduction technique in medicine. Purely medical problems and complexes are not subject to discussion. Deadline for the registration of lectures is March 15, 1960. Deadline for the registration of persons is Aug. 1, 1960. The program will be available in May, 1960. For information, write Deutsche Gesellschaft für Photographie eV. Neumarkt 49, Köln, Germany.

Air Pollution Conference Held in London.—North America's Air Pollution Control Association met with air pollution control groups representing countries from the other five continents in London Oct. 20-23 at the world's first International Clean Air Conference. The world-wide conference commemorated the 75th anniversary of the British Commonwealth's organized effort to promote clean air and the 60th anniversary of Great Britain's National Society for Clean Air. Chairman of the conference was Sir Hugh Beaver, English industrialist. The purpose of the international conference was to exchange information and promote international cooperation in the practical aspects of air pollution prevention and control. Subjects included international cooperation, research information exchange, and education in public relations phases of air pollution control.

Festival of Scientific Films in Paris.—The opening of the seventh session of the Permanent International Festival of Medico-Surgical and Scientific Motion Pictures, organized by La Gazette Medicale de France in cooperation with the National Association of the Motion Picture Producer Doctors and Scientists of France, will take place in Paris, Feb. 17, 1960, at the Faculte de Medecine. The producers of medicosurgical or scientific films of 16 mm. substandard format (exclusively) not shown in France before who wish to participate in this event should send their productions before Dec. 5, the date of the meeting of the Technical Council in charge of selecting the films, to the Association Nationale des Medecins Cinéastes et des Cinéastes

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Scientifiques de France, 23 Boulevard de Latour-Maubourg, Paris 7e. Foreign participants would find it advantageous to send their material through the cultural attache of their embassy in Paris, via their department of foreign affairs.

Pathology Meeting in London.—A meeting of the International Academy of Pathology will be held at the Royal College of Surgeons of England, Lincoln's Inn Fields, London, W. C. 2, England, June 20-24, 1960. The presentations will consist of the following: papers on June 20; on June 21 a slide seminar, "Proliferative Lesions of Breast," with professors C. Oberling of France, Robert W. Scarff, of London, and Lauren V. Ackerman, of St. Louis, as moderators; on June 22 an all-day symposium, "Pathophysiology and Pathology of the Kidney," by invited speakers; on June 23 and 24 a joint meeting of the American and British pathologists with a symposium on thyroiditis and cancer of the thyroid. Scientific exhibits will be accepted and visits to research centers will be arranged. There will be a social program for pathologists and their wives. For information, write Dr. Fathollah K. Mostofi, Secretary, International Academy of Pathology, Armed Forces Institute of Pathology, Washington 25, D. C.

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EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

AMERICAN BOARD OF ANESTHESIOLOGY: *Written.* Various locations, July 8. Final date for filing application is January 8. *Oral.* Miami Beach, April 25-30. Applications already on file. Sec., Dr. Forrest E. Leffingwell, 217 Farmington Ave., Hartford 5, Conn.

AMERICAN BOARD OF DERMATOLOGY: *Oral.* Oklahoma City, Jan. 15-18, 1960. The final date for filing all applications was July 1, 1959. Sec., Dr. Beatrice M. Kesten, One Haven Ave., New York 32.

AMERICAN BOARD OF INTERNAL MEDICINE: *Oral.* Philadelphia, March 11-12. Final date for filing application is January 15. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. New Haven, Nov. 14-16. Sec., Dr. Donald D. Matson, 300 Longwood Ave., Boston, Mass.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Part I, Written.* Chicago, January 16. Candidates notified of their eligibility to participate in the Part I examination must submit their case abstracts within thirty days of notification of eligibility. *Part II, Oral.* Chicago, April 11-16. Final date for filing application was August 1. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Written.* January 1960 in various cities. Applications for the 1960 written examination must be filed before July 1. *Oral.* 1960, San Francisco, May; Chicago, October. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Part II.* Chicago. Jan. 19-21, 1960. The deadline for the receipt of application was Aug. 15. *Part I.* Nashville, Denver and Philadelphia, Apr. 13-14. Deadline for receipt of applications is Nov. 30. Sec., Dr. Sam W. Banks, 116 South Michigan Ave., Chicago 3.

AMERICAN BOARD OF PATHOLOGY: New Orleans, Nov. 12-14. Final date for filing application was October 1. Sec., Dr. Edward B. Smith, Indiana University Medical Center, 1100 W. Michigan St., Indianapolis 7.

AMERICAN BOARD OF PATHOLOGY: *Examination in Forensic Pathology.* New Orleans, Nov. 13. Final date for filing application is October 1. Sec., Dr. Edward B. Smith, Indiana University Medical Center, 1100 W. Michigan St., Indianapolis 7.

AMERICAN BOARD OF PEDIATRICS: *Oral.* Washington, Dec. 4-6. *Written.* Jan. 8. Final date for filing application for the written examination is Dec. 1. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PHYSICAL MEDICINE AND REHABILITATION: *Oral and Written.* New York, June 17-18. Sec., Dr. Earl C. Elkins, Mayo Clinic, Rochester, Minn.

AMERICAN BOARD OF PLASTIC SURGERY: *Oral and Written.* Milwaukee, May 1960. Final date for filing application is January 1. Corresponding Secretary, Mrs. Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8, Mo.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York, Dec. 14-15; San Francisco, Mar. 14-15, 1960. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 was terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Examination.* Washington, Dec. 6-9. Deadline for filing application was July 1. Candidates examined in Diagnostic Roentgenology may expect to be examined in Physics. Obligatory examination in Nuclear Medicine has been postponed until after June 30, 1962 for those candidates being examined in Radiology or Therapeutic Radiology. Until that time the examination in Nuclear Medicine will be optional for those who wish to be examined in Radiology or Therapeutic Radiology. *Examination.* Cincinnati, Spring 1960. Deadline for filing applications is Jan. 1. A special examination in Nuclear Medicine (for those diplomates in Radiology or Therapeutic Radiology) will be offered provided there are sufficient applications. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written* examinations (Part 1) will be held on December 2, 1959 at various centers to be announced later. Closing date for filing applications was August 1. Those completing training requirements after September 30 cannot be considered for the Part I examination in December of the same year. *Oral examinations (Part II):* Boston, Dec. 14-15; Winston-Salem, No. Car., Jan. 18-19; New York, N. Y., Feb. 15-16; New Orleans, Mar. 14-15; Kansas City, Kans., May 16-17, and Los Angeles, May 19-20. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

AMERICAN BOARD OF UROLOGY: *Written.* Approximately 25 cities throughout the country, December 4, 1959. *Oral-Clinical* and *Examination in Pathology.* Chicago, February 1960. Final date for filing application was Sept. 1, 1959. Sec., Dr. William Niles Wishard, 30 Westwood Rd., Minneapolis 26, Minn.

DEATHS

Abbott, John Steele Ⓜ St. Paul, Minn.; University of Pennsylvania Department of Medicine, Philadelphia, 1908; served with the American Expeditionary Forces during World War I; formerly assistant professor of surgery at the University of Minnesota Medical School; past-president of St. Paul Surgical Society; from 1909 to 1912 assistant in surgery at the Mayo Clinic in Rochester, Minn.; retired from the Veterans Administration on April 30, 1956; formerly associated with the Ancker Hospital, Miller Hospital, and St. Luke's Hospital, where he died Aug. 10, aged 75.

Adams, William Bradford, Owls Head, Maine; Harvard Medical School, Boston, 1918; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; veteran of World War I; formerly practiced in Springfield, Mass., where he was associated with the Shriners' Hospital for Crippled Children, Health Department Hospital, and Wesson Maternity Hospital; died Aug. 16, aged 69.

Anderson, Stewart Harry Ⓜ Kerrville, Texas; University of Illinois College of Medicine, Chicago, 1915; veteran of World War I; served on the staff of the Veterans Administration Hospital; died in the Sid Peterson Memorial Hospital Aug. 3, aged 69.

Armington, Herbert Hamlin Ⓜ Providence, R. I.; Columbia University College of Physicians and Surgeons, New York City, 1904; veteran of World War I; at one time school physician; formerly staff member of the Providence Lying-in Hospital and the Rhode Island Hospital; died in the Veterans Administration Hospital Aug. 11, aged 81.

Baron, Benzion Chaim Ⓜ Munising, Mich.; Northwestern University Medical School, Chicago, 1930; formerly member of the board of education; past-president of the Munising Rotary Club; veteran of World War II; on the staff of Munising Hospital; died in Palmer Aug. 3, aged 53.

Bartruff, Charles Henry Ⓜ Reinbeck, Iowa; Drake University College of Medicine, Des Moines, 1913; served overseas during World War I; staff member of the Grundy County Memorial Hospital in Grundy Center; died Aug. 24, aged 71.

Bassler, Anthony Ⓜ New York City; born in New York City May 24, 1874; Bellevue Hospital Medical College, New York City, 1898; successively lecturer in pediatrics, pathology, and internal medicine at his alma mater from 1900 to 1910; for many years on the faculty at New York Polyclinic Medical School and Hospital and Fordham University School of Medicine; specialist certified by the American Board of Internal Medicine; first chairman and founder in 1917-1918 of the Section on Gastroenterology, American Medical Association; past-president of the National Gastroenterological Association, National Society for the Advancement of Gastroenterology, New York Gastroenterological Association, American Physicians Art Association, and the New York City Physicians Golfing Association, of which he was one of the founders; served as American president of the International Society of Gastroenterology, which he helped organize, for which France gave him the Legion of Honor, and president of the American delegation to the International Congress on Hepatic Insufficiency in Vichy, France, in September, 1937; an honorary vice-president of the American Society of Stomatology; member of the American College of Gastroenterology, of which he was one of the founders and first president, the Endocrine Society, and the American Roentgen Ray Society; fellow of the American College of Physicians; honorary member of the Belgium Gastroenterological Society; cited by the Navy for his work on dysentery in World War I; also cited by the Army for his aid to the Selective Service; consultant in gastroenterology, Doctors, Misericordia, and St. Vincent's hospitals and New York Polyclinic Medical School and Hospital in New York City, St. John's Riverside Hospital, Yonkers, St. Agnes Hospital, White Plains, United Hospital, Port Chester, New Rochelle (N. Y.) Hospital, and the Yonkers Professional Hospital in Yonkers; co-editor of the *Review of Gastroenterology* which dedicated its November-December, 1939, issue to him in honor of his sixty-fifth birthday; on June 9, 1938, received the honorary degree of doctor of laws from the Hahnemann Medical College of Philadelphia; author of books in his speciality and contributed much to periodic literature; collaborator in fine systems of medicine; died Aug. 20, aged 85.

Bell, Aaron Ⓜ New York City; Cornell University Medical College, New York City, 1926; specialist certified by the American Board of Psychiatry and Neurology, Inc.; member of the American Academy of Neurology and the Association for Research in Nervous and Mental Disease; psychiatrist of the New York State Department of Mental Hygiene; served as director of neuropsychiatry at Lenox Hill Hospital and as consulting neurologist at the Huntington (N. Y.) and Hasbrouck Heights (N. J.) hospitals; died Aug. 26, aged 57.

Ⓜ Indicates Member of the American Medical Association.

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Benefield, Charles Edward Ⓜ Fort Smith, Ark.; Memphis (Tenn.) Hospital Medical College, 1902; died Aug. 6, aged 88.

Bixby, Edward Welles Ⓜ Wilkes-Barre, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1911; fellow of the American College of Physicians; member of the American Trudeau Society; past-president of the Luzerne County Medical Society; served in France during World War I; served on the staffs of the Wilkes-Barre General Hospital and the White Haven (Pa.) Sanatorium; died at Glen Summit Aug. 21, aged 73.

Blake, Albert Julian Ⓜ Paterson, N. J.; Harvard Medical School, Boston, 1937; interned at St. Joseph's Hospital; served a residency at the Hopedell Hospital in Preakness, N. J.; veteran of World War II; an examining physician in Paterson's public schools; on the courtesy staff of the Barnert Memorial Hospital, where he died Aug. 24, aged 48.

Blakeley, Arthur C. Ⓜ Detroit; Detroit College of Medicine, 1911; associated with the Veterans Administration; died Aug. 20, aged 75.

Blum, Samuel George, Brooklyn; Cornell University Medical College, New York City, 1909; on the staff of the Jewish Hospital; died Aug. 23, aged 73.

Breuer, Robert Eugene Ⓜ Rolla, Mo.; St. Louis University School of Medicine, 1907; member of the American Academy of General Practice; for many years member of the Phelps County Highway Commission; past-vice-president of the Missouri State Medical Association; for many years a member of the school board of Newburg; first chief of staff at the Phelps County Memorial Hospital, where he died Aug. 19, aged 77.

Broman, Martin Robert Ⓜ Evanston, Ill.; Rush Medical College, Chicago, 1916; certified by the National Board of Medical Examiners; fellow of the American College of Surgeons; veteran of World War I; in 1957 retired as pathologist at the Swedish Covenant Hospital in Chicago; died in Evanston Hospital Aug. 16, aged 66.

Bryant, J. Trevor Ⓜ Seattle; University of Oregon Medical School, Portland, 1940; interned at the French Hospital in San Francisco; certified by the National Board of Medical Examiners; associated with the Seattle General Hospital; died in the Swedish Hospital Aug. 26, aged 46.

Byers, Guy Ewing Gilfillan Ⓜ Salem, Ohio; Western Reserve University School of Medicine, Cleveland, 1918; served a term on the city board of health; past-president of the Columbiana County Public Health League; on the staff of the Salem City Hospital; past-president of the Salem Rotary Club; died Aug. 21, aged 67.

Caldwell, Hugh McIntyre Ⓜ Columbus, Wis.; Rush Medical College, Chicago, 1924; on the staff of St. Mary's Hospital; died in August, aged 59.

Carey, Michael Joseph, Council Bluffs, Iowa; St. Louis University School of Medicine, 1926; for many years on the faculty of Creighton University School of Medicine in Omaha; associated with the Veterans Administration Center in Des Moines; died in St. Joseph's Hospital in Omaha June 12, aged 62.

Cassidy, Patrick Homer, Salinas, Calif.; University of Washington School of Medicine, Seattle, 1958; interned at the University of Kansas Medical Center in Kansas City, Kan.; resident physician at the Monterey County Hospital; died Aug. 2, aged 36.

Chunn, Barker Daniel Ⓜ Beaumont, Texas; University of Texas School of Medicine, Galveston, 1934; interned at St. Therese Hospital; associated with Baptist Hospital of Southeast Texas, Hotel Dieu Hospital, and St. Therese Hospital; died Aug. 8, aged 52.

Clark, John Neal Ⓜ Vallejo, Calif.; University of California School of Medicine, San Francisco, 1941; interned at St. Mary's Hospital, where he served a residency; served a residency at the Solano County Hospital in Fairfield; member of the American Academy of General Practice; assistant health officer of Solano County; died Aug. 16, aged 47.

Coppridge, William Maurice Ⓜ Durham, N. C.; born in Danville, Va., July 24, 1893; Jefferson Medical College of Philadelphia, 1918; president of the American Urological Association and past-president of the Southeastern Section; specialist certified by the American Board of Urology; fellow of the American College of Surgeons; past-president of the North Carolina Urological Association, Medical Society of State of North Carolina, and the Durham–Orange Counties Medical Society; served as a member of the state board of medical examiners; for many years clinical professor of surgery at the University of North Carolina School of Medicine, Chapel Hill; formerly a member of the commission to study needs of medical education in North Carolina; veteran of World War I; a member of the North Carolina Committee for Procurement and Assignment of Physicians in Armed Forces during World War II; a member the county board of health; served as director of the laboratory of urology and chief of urology staff at Watts Hospital; died in the New England Baptist Hospital, Boston, Aug. 28, aged 66.

Craig, Marion Stark Ⓜ Batesville, Ark.; Vanderbilt University School of Medicine, Nashville, Tenn., 1911; for many years owned and operated the Craig Hospital; a director of the Batesville Federal Savings and Loan Association; died Aug. 20, aged 74.

Degenring, Anna J., Elizabeth, N. J.; Woman's Medical College of Pennsylvania, Philadelphia, 1904; for many years a medical missionary in India; died in Springfield Aug. 28, aged 86.

Dix, George Alfred Ⓜ Worcester, Mass.; Harvard Medical School, Boston, 1899; veteran of World War I; served on the staff of the Worcester City Hospital; consultant on the medical board of the Memorial Hospital, where he died Aug. 20, aged 87.

Donald, Dan Caldwell Ⓜ Birmingham, Ala.; Tulane University School of Medicine, New Orleans, 1911; fellow of the American College of Surgeons; clinical professor of surgery at the Medical College of Alabama; past-president of the Jefferson County Medical Society; associated with Birmingham Baptist Hospital and the University Hospital; past-president of the Society of Medical History; died Aug. 21, aged 71.

Dozier, Byron T., Dallas, Texas; Barnes Medical College, St. Louis, 1897; died Aug. 19, aged 84.

DuVall, William Nelson Ⓜ Mishawaka, Ind.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1900; Bennett College of Eclectic Medicine and Surgery, Chicago, 1901; associated with St. Joseph's Hospital, where he died Aug. 20, aged 85.

Ehrlich, Ralph Louis, St. Louis; Washington University School of Medicine, St. Louis, 1925; formerly on the staff of the Robert Koch Hospital in Koch; on the staff of St. Anthony's Hospital; died in Maplewood Aug. 23, aged 59.

Evans, Claude Monroe, Marshall, Ark.; St. Louis University School of Medicine, 1909; died Aug. 13, aged 78.

Fama, Charles Ⓜ New York City; New York Homeopathic Medical College and Hospital, New York City, 1914; an honorary surgeon of the New York Police Department; served on the U. S. Board of Pension Surgeons and as a member of the medical board of the New York City Employees Retirement System; on the staff of the Union Hospital; died Aug. 29, aged 70.

Ferrell, George Stone Ⓜ Lynchburg, Va.; Medical College of Virginia, Richmond, 1940; veteran of World War II; interned at the Norwalk (Conn.) General Hospital and the Memorial Hospital in Wilmington, Del.; served a residency at the Sibley Memorial Hospital in Washington, D. C., St. Mary's Hospital in Grand Rapids, Mich., and the Riverside Hospital in Newport News, Va.; staff member of the State Hospital at Morganton, N. C., where he died Aug. 28, aged 46.

Frazier, Frederick Gary Ⓜ Chicago; Meharry Medical College, Nashville, Tenn., 1915; veteran of World War I; died in the Veterans Administration Hospital in Hines, Ill., Aug. 26, aged 71.

Frothingham, Channing, Boston; born in Brooklyn May 10, 1881; Harvard Medical School, Boston, 1906; past-president of the Massachusetts Medical Society; member of the Association of American Physicians; veteran of World War I; served on the faculty of his alma mater; overseer at Harvard College from 1936 to 1942; specialist certified by the American Board of Internal Medicine; trustee, Boston Psychopathic Hospital; consulting physician at the Eastern Maine General Hospital in Bangor, Maine, and the Faulkner Hospital; emeritus consulting physician at the Peter Bent Brigham Hospital; chairman of the Committee of Physicians for Improvement of Medical Care, Inc., from 1941 to 1947; chairman of the Committee for the Nation's Health; died in the Massachusetts General Hospital Aug. 11, aged 78.

Fuqua, Harold Boyd Ⓜ Terre Haute, Ind.; University of Illinois College of Medicine, Chicago, 1939; interned at the U. S. Marine Hospital in New Orleans; veteran of World War II and the Korean War; on the staff of the Union Hospital; died Aug. 13, aged 50.

Gardner, Leo Lloyd, Coral Gables, Fla.; Baltimore Medical College, 1907; formerly practiced in Chicago; died in the Jackson Memorial Hospital in Miami Aug. 18, aged 76.

Germain, Rodolphe T., Spokane, Wash.; University of Montreal Faculty of Medicine, Montreal, Que., Canada, 1896; died Aug. 15, aged 84.

Gilden, A. Morris Ⓜ Buffalo, N. Y.; University of Buffalo School of Medicine, 1920; associated with the Buffalo General Hospital; died in Hamilton, Ont., Canada, Aug. 16, aged 65.

Glass, Earl Floyd Ⓜ Wheeling, W. Va.; College of Physicians and Surgeons, Baltimore, 1907; associated with the Wheeling and Ohio Valley General hospitals; died Aug. 15, aged 80.

Gooder, William Verner Ⓜ Marengo, Ill.; Northwestern University Medical School, Chicago, 1905; veteran of World War I; died in Chicago Aug. 10, aged 78.

Gregg, Orion Russell Ⓜ Norman, Okla.; Kansas City (Mo.) Hahnemann Medical College, 1908; veteran of World War I; died Aug. 21, aged 74.

Grivelis, Evangel Ⓜ Brooklyn; University and Bellevue Hospital Medical College, New York City, 1931; associated with St. John's Episcopal Hospital; died Aug. 19, aged 68.

Hahn, Theodore F., De Land, Fla.; Baltimore Medical College, 1902; for many years a Presbyterian minister; a retired medical missionary; died in the Fish Memorial Hospital Aug. 20, aged 82.

Hamlin, Roscoe Earl, Santa Rosa, Calif.; College of Physicians and Surgeons of San Francisco, 1907; died Aug. 12, aged 80.

Harding, Samuel Asberry, Mocksville, N. C.; North Carolina Medical College, Charlotte, 1910; died in the North Carolina Baptist Hospital, Winston-Salem, Aug. 22, aged 71.

Hayman, Philip Paul Ⓜ Teaneck, N. J.; College of Physicians and Surgeons, Baltimore, 1911; died July 6, aged 71.

Hemminger, Edward F. Ⓜ Upper Darby, Pa.; Jefferson Medical College of Philadelphia, 1908; specialist certified by the American Board of Otolaryngology; on the draft board during World War II; served on the faculty of his alma mater; during his career served on the staffs of the Jefferson Hospital in Philadelphia, Bryn Mawr (Pa.) Hospital, and the Veterans Administration Hospital in Coatesville; died in the Delaware County Hospital in Drexel Hill Aug. 27, aged 76.

Hinshaw, Jonathan Dixon Ⓜ Canon City, Colo.; Kansas City (Mo.) Medical College, 1903; served as mayor; died Aug. 19, aged 85.

Hitchcock, Ethel Olivia Hunter, New York City; Cornell University Medical College, New York City, 1902; died May 22.

Holtzmuller, Charles William Ⓜ Farmersville, Ohio; Eclectic Medical Institute, Cincinnati, 1899; for many years president of the Citizens Bank of Farmersville; died Aug. 13, aged 85.

Jameson, Curtiss Norton Ⓜ Rochester, N. Y.; Rush Medical College, Chicago, 1902; veteran of World War I; associated with the Genesee and Rochester General hospitals; member of the American Society of Anesthesiologists, Inc.; died Aug. 22, aged 82.

Johnen, Arthur, West Norwalk, Conn.; Eclectic Medical College of the City of New York, 1897; died in the Norwalk (Conn.) Hospital Aug. 11, aged 98.

Kirkland, Luman Wilbur Ⓜ Beeville, Texas; Medical College of Alabama, Mobile, 1904; for many years county health officer; member of the American Trudeau Society; associated with the Beeville Hospital and the Thompson Memorial Hospital; on the board of directors of the Texas Tuberculosis Association; died Aug. 20, aged 77.

McClellan, Henry Joseph, St. Petersburg, Fla.; Baltimore University School of Medicine, 1898; died Aug. 10, aged 92.

Mahood, William Richmond, Santa Barbara, Calif.; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1903; formerly practiced in Sioux City, Iowa; served on the staff of the Santa Monica (Calif.) Hospital; died Aug. 24, aged 83.

Marshall, Ernest Jones, Kansas City, Mo.; Northwestern University Medical School, Chicago, 1927; associated with the Wheatley-Provident Hospital and the Kansas City General Hospital; died Aug. 21, aged 74.

Martin, Clement Leon Ⓜ Chicago; born in Omaha March 9, 1891; Creighton University School of Medicine, Omaha, 1916; formerly a fellow in surgery at the Mayo Clinic, Rochester, Minn., where he was associate in the department of proctology; assistant professor of applied anatomy at his alma mater and on the surgical staff of St. Joseph's Hospital in Omaha from 1923 to 1926; clinical professor of proctology at Loyola University School of Medicine from 1927 to 1957; from 1948 to 1952 trustee of the Chicago Medical Society and past-president of the North Shore Branch; fellow, and in 1938-1939 vice-president of the American Proctologic Society; member of the International Board of Trustees, International College of Surgeons since 1952, since 1956 treasurer, and regent for Illinois of the U. S. Chapter, 1952-1953; fellow of the American College of Surgeons; member of the Institute of Medicine of Chicago and the Association of Military Surgeons of the United States; specialist certified by the American Board of Surgery; founder member, American Board of Proctology; director of proctologic division, Loyola-Mercy Clinics from 1939 to 1957; for many years consulting proctologist, City of Chicago Municipal Tuberculosis Sanitarium, Veterans Administration Hospital in Hines, Ill., Columbus Hospital, Oak Park (Ill.) Hospital, St. Bernard's Hospital, Alexian Brothers Hospital, and the Veterans Regional Office; senior attending proctologist, Mercy Hospital; died in the Presbyterian-St. Luke's Hospital Aug. 15, aged 68.

Mazur, Herbert Arthur Ⓜ St. Louis; Washington University School of Medicine, St. Louis, 1943; interned at Jewish Hospital in St. Louis; served a residency at St. Louis County Hospital in Clayton, Mo., and St. Louis Children's Hospital; instructor of clinical pediatrics at his alma mater; veteran of World War II; member of the American Academy of Pediatrics; specialist certified by the American Board of Pediatrics; staff member of Barnes and Children's hospitals and Jewish Hospital, where he died Aug. 23, aged 40.

Miller, George Louis, San Diego, Calif.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1902; died Aug. 12, aged 82.

Morell, Charles Joseph Ⓜ Philadelphia; Medico-Chirurgical College of Philadelphia, 1907; also a graduate in pharmacy; died in the Graduate Hospital of the University of Pennsylvania Aug. 26, aged 83.

Morgan, Harry Price, Wood River, Ill.; Bennett College of Eclectic Medicine and Surgery, Chicago, 1906; associated with the Wood River Township Hospital, where he died Aug. 14, aged 78.

Morrison, Winfield Scott Ⓜ Minonk, Ill.; the Hahnemann Medical College and Hospital, Chicago, 1905; for many years secretary of the Woodford County Medical Society; formerly county coroner; served as secretary of the board of education and the Woodford County Tuberculosis Association; for many years local surgeon of the Illinois Central Railroad; member of the Chamber of Commerce; in 1955 the Minonk Community honored him with "Dr. Morrison's Day" on July 4; associated with St. Mary's Hospital in Streator; died near Dana Aug. 17, aged 78.

Munger, Irvia Clarence Sr. Ⓜ Lincoln, Neb.; Illinois Medical College, Chicago, 1900; veteran of World War I; fellow of the American College of Surgeons; died Aug. 13, aged 84.

Munson, Leonard W., Milford, Conn.; Georgetown University School of Medicine, Washington, D. C., 1896; served on the staff of the Stamford (Conn.) Hospital; formerly medical examiner for Metropolitan Life Insurance Company; died Aug. 8, aged 90.

Nelson, Bendet, New York City; University of St. Vladimira Faculty of Medicine, Kiev, Russia, 1897; died June 19, aged 91.

Niedermeyer, Frederick Pierce Ⓜ Kansas City, Mo.; Northwestern University Medical School, Chicago, 1948; interned at St. Joseph's Hospital, where he served a residency; member of the American Academy of General Practice; veteran of World War II; served as a major in the U. S. Air Force Reserve; died Aug. 12, aged 36.

Opre, Harry E., Miami, Fla.; Chicago College of Medicine and Surgery, 1908; veteran of the Spanish–American War; died Aug. 9, aged 80.

Pamment, Harry Gill Ⓜ Toledo, Ohio; Rush Medical College, Chicago, 1913; served for 25 years as part-time epidemiologist for the city of Toledo health department; died Aug. 17, aged 74.

Patterson, Charles Henry, Lynchburg, Va.; University of Pennsylvania School of Medicine, Philadelphia, 1930; member of the American Academy of Dermatology and Syphilology; veteran of World War II; associated with the Lynchburg Training School and Hospital in Colony, and Virginia Baptist and Lynchburg General hospitals; died Aug. 9, aged 54.

Pavlidis, Isaac Michael, Havertown, Pa.; American University of Beirut School of Medicine, Syria, 1908; died in the Bryn Mawr (Pa.) Hospital Aug. 16, aged 82.

Pearce, Louise, Bell Mead, N. J.; born in Winchester, Mass., March 5, 1885; Johns Hopkins University School of Medicine, Baltimore, 1912; in 1941 appointed a member of the board of corporators, and from 1946 to 1951 president of the Woman's Medical College of Pennsylvania, where in 1952 she received a citation; received the Order of the Crown of Belgium for conducting the African sleeping sickness mission in the Belgian Congo in 1920-1921, sponsored by the Rockefeller Institute, with which she was associated for many years; visiting professor of syphilology at the Peiping Union Medical College in Peiping, China, 1931-1932; for many years a member of the general advisory council of the American Social Hygiene Association; member of the American Association of Pathologists and Bacteriologists and the American Society for Experimental Pathology; a trustee of the New York Infirmary, which in 1951 honored her with the Elizabeth Blackwell citation for achievement in medicine; from 1940 to 1946 a member of the board of Princeton (N. J.) Hospital; held honorary degrees from Wilson College, Bucknell University, Skidmore College, and the Woman's Medical College; died in the New York Hospital Aug. 10, aged 74.

Pearl, Nathaniel Ⓜ Long Beach, N. Y.; L. R. F. P. & S., of Glasgow, 1938; L. R. C. P., of Edinburgh, and L. R. C. S., of Edinburgh, Scotland, 1939; member of the American Academy of General Practice; veteran of World War II; associated with the Long Beach Memorial Hospital; died Aug. 6, aged 52.

Peete, Charles Henry Sr. Ⓜ Warrenton, N. C.; University of Virginia Department of Medicine, Charlottesville, 1903; served on the selective service boards during World Wars I and II; died Aug. 19, aged 80.

Person, Reuben Edward, Ola, Ark.; (licensed in Arkansas in 1903); died in St. Mary's Hospital, Russellville July 10, aged 78.

Pipes, David McKowen Ⓜ Baton Rouge, La.; Tulane University School of Medicine, New Orleans, 1934; member of the American College of Allergists; associated with the Baton Rouge Hospital and Our Lady of the Lake Hospital; died Aug. 25, aged 54.

Prunskis, Vladas, Chicago; Vytauto Didziojo Universiteto Medicinos Fakulteto, Kaunas, Lithuania, 1941; interned at the St. Elizabeth Hospital, where he was a member of the staff; died in the Albert Merritt Billings Hospital Aug. 21, aged 46.

Ransom, Harry Ensign Ⓜ Des Moines, Iowa; born in Avalon, Wis., Oct. 16, 1885; Marquette University School of Medicine, Milwaukee, 1914; city health commissioner from 1932 to 1951; assistant health officer from 1922 to 1932; served as secretary of the Polk County Medical Society, which in 1952 presented a bronze plaque in his honor to the city of Des Moines in recognition of his thirty years of efficient effort in establishing a modern health serv-

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ice for the city of Des Moines and surrounding community; veteran of World War I; associated with the Broadlawns Polk County Hospital, Iowa Lutheran Hospital, Mercy Hospital, and the Iowa Methodist Hospital, where he died Aug. 10, aged 73.

Reingold, Alexander, North Bergen, N. J.; University and Bellevue Hospital Medical College, New York City, 1914; for many years practiced in Hoboken; veteran of World War I; died Aug. 24, aged 67.

Renard, Suzanne Gesmar, New York City; Université de Paris Faculté de Médecine, France, 1922; made a Chevalier of the French Legion of Honor for nursing duties among French troops during World War I; died in Geneva, Switzerland Aug. 3, aged 71.

Rigby, Samuel B., Fairview, Utah; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1917; served four terms as mayor and five terms as Sanpete County commissioner; associated with Sanpete Latter-Day Saints Hospital in Mount Pleasant; died Aug. 7, aged 71.

Rosove, Leon Ⓜ Los Angeles; University of California School of Medicine, San Francisco, 1931; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; veteran of World War II; associate clinical professor of medicine, University of California at Los Angeles School of Medicine; associated with the Los Angeles County Hospital and the Veterans Administration Center; died Aug. 11, aged 53.

Rudell, Gustave Leander Ⓜ Minneapolis; University of Minnesota Medical School, Minneapolis, 1906; veteran of World War I; died Aug. 8, aged 83.

Sayre, Philip Preston Ⓜ Onsted, Mich.; University of Michigan Homeopathic Medical School, Ann Arbor, 1914; past-president of the Lenawee County Medical Society and the Van Buren County Medical Society; associated with the Emma L. Bixby Hospital, Adrian, where he died Aug. 13, aged 73.

Scales, Emmet Thomas Ⓜ Des Moines, Iowa; State University of Iowa College of Medicine, Iowa City, 1927; member of the Endocrine Society and the American Academy of General Practice; at various times on the staffs of the Mercy, Broadlawns, and Iowa Lutheran hospitals; died Aug. 10, aged 58.

Shook, Ralph William Ⓜ Kalamazoo, Mich.; University of Michigan Medical School, Ann Arbor, 1927; for many years councilor of the Michigan State Medical Society; past-president of the Kalamazoo Academy of Medicine; served as lieutenant colonel in the Army Medical Corps in England during World War II; died in the James Decker Munson Hospital in Traverse City Aug. 9, aged 56.

Smith, Benjamin Averill Ⓜ Huntington, W. Va.; (licensed in West Virginia in 1897); died Aug. 11, aged 92.

Smith, Brainard Sutton Ⓜ Shaker Heights, Ohio; Harvard Medical School, Boston, 1954; interned at the New York Hospital in New York City; served a residency in pediatrics at the Cincinnati General Hospital and the Children's Hospital in Cincinnati; resident pediatrician at the Children's Hospital in Detroit; certified by the National Board of Medical Examiners; relieved as a captain in the medical corps of the U. S. Army Reserve in June, 1957; died in St. Luke's Hospital in Cleveland Aug. 22, aged 31.

Smith, Ellsworth Johnson, Madison, Conn.; Columbia University College of Physicians and Surgeons, New York City, 1904; veteran of World War I; formerly practiced in Larchmont, N. Y.; served on the staff of the New Rochelle (N. Y.) Hospital; member of the local health board; died Aug. 6, aged 80.

Sterns, Albert Henry Ⓜ New Bedford, Mass.; Tufts College Medical School, Boston, 1920; a member of the staff of St. Luke's Hospital, where he died Aug. 7, aged 65.

Stinchfield, Walter Scott Ⓜ Skowhegan, Maine; Bellevue Hospital Medical College, New York City, 1896; past-president and treasurer of the Maine Medico-Legal Society; for many years county medical examiner; died in the Redington Memorial Hospital Aug. 8, aged 86.

Stroud, William Daniel Ⓜ Philadelphia; born in Villanova, Pa., Nov. 20, 1891; University of Pennsylvania School of Medicine, Philadelphia, 1916; secretary of the Section on the Practice of Medicine of the American Medical Association from 1940 to 1944, when he became chairman, serving until 1946; specialist certified by the American Board of Internal Medicine; member of the Association of American Physicians, and the American Clinical and Climatological Association; fellow of the American College of Physicians, of which he served as treasurer; past-president of the American Heart Association and the Philadelphia Heart Association; assistant professor of clinical medicine at the University of Pennsylvania School of Medicine and professor of cardiology at the University of Pennsylvania Graduate School of Medicine; member of the board of directors of the Philadelphia Health Council and Tuberculosis Committee; veteran of World War I; chief of staff, Children's Heart Hospital; consulting cardiologist at the Abington (Pa.) Memorial Hospital, Norristown (Pa.) State Hospital, Bryn Mawr (Pa.) Hospital, St. Christopher's Hospital, and the Pennsylvania Hospital; editor of "The Diagnosis and Treatment of Cardiovascular Disease"; died in the Bryn Mawr (Pa.) Hospital Aug. 19, aged 67.

Sweet, Frank R., North Little Rock, Ark.; (licensed in Arkansas in 1903); died Aug. 7, aged 82.

Thomas, William Nelson Ⓜ Oxford, N. C.; Medical College of Virginia, Richmond, 1911; county health officer; for a long period county coroner; a member of the board of City Commissioners, Oxford Board of Graded School Trustees and Oxford Fire Department of which he was formerly chief; a director of Union National Bank, Oxford Building and Loan Association, and a charter member of the Oxford Rotary Club; associated with the Granville Hospital, where he died Aug. 3, aged 71.

Thompson, George Letcher Ⓜ Owensboro, Ky.; University of Louisville Medical Department, 1907; served as health officer of Owensboro, and McLean and Daviess counties; veteran of World War I; on the courtesy staff of the Owensboro-Daviess County Hospital, where he died Aug. 10, aged 81.

Trumpeter, John Horace Ⓜ Beaver, Pa.; University of Pittsburgh School of Medicine, 1922; specialist certified by the American Board of Obstetrics and Gynecology; past-president of the Beaver County Medical Society; formerly on the faculty of his alma mater; associated with the Beaver Valley General Hospital in New Brighton, Providence Hospital, Beaver Falls, and the Rochester (Pa.) General Hospital, where he died Aug. 9, aged 62.

Tyrrell, George Washington Ⓜ Perth Amboy, N. J.; College of Physicians and Surgeons, Baltimore, 1893; associated with the Perth Amboy Hospital; died in Keyport July 1, aged 89.

Uthoff, Carl Woodrow Ⓜ Grand Rapids, Mich.; Western Reserve University School of Medicine, Cleveland, 1943; interned at the University Hospital in Cleveland; served a residency at the Mercy Hospital in Toledo, Ohio; veteran of World War II; on the staff of the Butterworth Hospital; died Aug. 17, aged 42.

Vander Veer, Adrian Holt Ⓜ Chicago; born in New York City Nov. 4, 1909; Columbia University College of Physicians and Surgeons, New York City, 1934; interned at the Bellevue Hospital in New York City; served a residency at the Michael Reese Hospital; specialist certified by the American Board of Psychiatry and Neurology, Inc.; certified by the National Board of Medical Examiners; member of the American Psychoanalytic Association and the American Psychiatric Association; past-president of the Chicago Council of Child Psychiatry; at one time on the faculty of Rush Medical College and the University of Chicago, The School of Medicine; served on the staff of the Cook County Psychopathic Hospital; died in the Michael Reese Hospital Aug. 13, aged 49.

Warrick, Will Carleton, Pontiac, Mich.; University of Illinois College of Medicine, Chicago, 1914; served on the staff of the Pontiac General Hospital, where he died July 25, aged 71.

Waters, Chester Thomas, Dallas, Texas; Louisville (Ky.) and Hospital Medical College, 1908; for many years associated with the Veterans Administration; died Aug. 11, aged 71.

Watts, Wilbur Ⓜ Trenton, N. J.; University of Pennsylvania Department of Medicine, Philadelphia, 1907; specialist certified by the American Board of Otolaryngology; veteran of World War I; associated with St. Francis Hospital, where he served as president of the staff and chief of otolaryngology; died Aug. 12, aged 75.

Webb, Jonathan Warner, Parkersburg, W. Va.; Baltimore University School of Medicine, 1905; died July 22, aged 82.

Welch, Robert Sellman Gray Ⓜ Annapolis, Md.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1917; past-president of the Anne Arundel County Medical Society; fellow of the American Academy of Ophthalmology and Otolaryngology; served in the regular U. S. Navy; veteran of World War I; for years served as chairman of the Anne Arundel Welfare Board; associated with the Anne Arundel General Hospital, where he died Aug. 5, aged 66.

Welch, Winthrop Sherwood Ⓜ Torrington, Conn.; Cornell University Medical College, New York City, 1941; interned at the Hartford (Conn.) Hospital, where he served a residency; medical officer in a combat infantry unit in the Pacific Theater during World War II; associated with the Charlotte Hungerford Hospital; died July 20, aged 46.

Wentworth, Daniel Webster, St. Petersburg, Fla.; Medical School of Maine, Portland, 1899; veteran of World War I; died in Eliot, N. H., July 29, aged 89.

Williams, Harold Otis Ⓜ Kendallville, Ind.; Indiana University School of Medicine, Indianapolis, 1913; member of the American Academy of General Practice; past-president of the Twelfth District of the Indiana State Medical Association and the Noble County Medical Society; for many years member of the city council; veteran of World War I; surgeon for the New York Central and Pennsylvania railroads; physician for the police department; associated with the McCray Memorial Hospital, where he died Aug. 1, aged 69.

Wilson, James Cathcart, Holly Hill, Fla.; Columbia University College of Physicians and Surgeons, New York City, 1922; served on the staff of the Lawrence Hospital in Bronxville, N. Y.; died in the Halifax District Hospital, Daytona Beach, Aug. 23, aged 61.

Wolfson, Isaac Edward Ⓜ Los Angeles; University of Cincinnati College of Medicine, 1931; veteran of World War II; died in the Cedars of Lebanon Hospital July 20, aged 54.

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FOREIGN LETTERS

BELGIUM

Roentgenography of the Prostate.—Roentgenographic studies of the prostate are still rarely made. Blum and Sichel (*Acta urologica belgica*) described a new technique for such studies. Tomograms of the prostate are made after filling the bladder with 100 to 150 cc. of air, oxygen, or carbon dioxide. Because of the simplicity and safety of this method it should become the method of choice. It provides information about the size and form of adenomas not easily perceptible on rectal examination and helps to establish precise diagnosis of epithelioma of the prostate by exactly determining the degree of endocystic invasion. In case of a prostatic abscess tomography shows unsuspected aspects of deviation of the affected lobe and compression of the nonaffected lobe.

Detection of Alcoholic Intoxication.—In detecting alcoholic intoxication, particularly that involving automobile accidents, there has been a tendency for some time to estimate the level of alcohol in the blood by analysis of the expired air. Moreau and co-workers reported at the Academie de Médecine that the method of Schuhe and Frey deserves to be looked on as a preliminary test by which alcoholic intoxication may be excluded, thus making blood tests unnecessary if the suspicion is confirmed. Comparing the results of this test with those obtained by blood analysis has shown, however, that there are great variations depending on whether the subject breathes merely until a certain signal lamp has been lighted as recommended or with maximum expiration. In the latter case the chances that the automatic dosage will affect the alveolar air rather than the bronchial air are increased and the agreement with the blood level becomes better as a result. Reliance on an analysis of the expired air is therefore not justifiable.

Atypical Myocardial Infarction.—Ghys (*Acta cardiologica*) reported a series of 248 patients with myocardial infarction. The physician should know that among the patients with myocardial infarction 5 to 10% are atypical in that no pain is associated with the lesion. The absence of pain in those patients can be explained either by the destruction of the sensory endings in the infarcted zone or by the impermeability of the synapses of the posterior horn of the spinal cord to cardiac stimuli. On the other hand, pain is manifested in an atypical localization in a fair percentage of the patients. There may be acute pain in the epigastrium associated with abdominal rigidity leading to unnecessary and even dangerous laparotomy. Apparent indications for an immediate operation should not interfere with obtaining an electrocardiogram in patients with symptoms suggestive of a perforated peptic ulcer. Furthermore a significant number of patients with myocardial infarction do not show pathognomonic electrocardiographic manifestations, because of either ventricular tachycardia or a disturbance in the atrioventricular conduction (bundle-branch block). It is important, therefore, to investigate carefully both subjective and objective signs of myocardial infarction in patients who suddenly present atrioventricular or interventricular heart block.

The items in these letters are contributed by regular correspondents in the various foreign countries.

BRAZIL

Hibernotherapy for Eclampsia.—A series of 30 patients with eclampsia were given a lytic cocktail by Dr. Caetano Giordano and co-workers (*Revista de ginecologia e d'obstetricia*, July, 1959). Artificial hibernation had no statistical or clinical advantages over treatment with magnesium sulfate, as regards the disappearance of convulsive crises or maternal and fetal mortality, nor was it effective in combating hypertension.

Schistosomiasis.—Dr. J. Pelegrino and co-workers of the University of Minas Gerais (*Jornal de Pediatria*, May, 1959) compared the results obtained by stool examination with those obtained by intradermal tests using adult schistosome antigen and quantitative complement-fixation tests for the diagnosis of intestinal schistosomiasis. The observations were made on 234 unselected school children aged from 10 to 15 years and living in an endemic area near Belo Horizonte. Stool examination was repeated up to four times in those children presenting negative first stool examinations and positive or doubtful immunological tests. Rectal biopsy was performed on those with repeated negative stool examination. Positive results were obtained in 59.4% of the stool examinations, 42.7% of the intradermal tests on the forearm, 59% of the intradermal tests on the back, and 66.7% of the complement-fixation tests.

Clinical examination of 63 infected and 48 noninfected children showed the difficulties of clinical diagnosis of this disease. The authors suggested the following schedule for the diagnosis of intestinal schistosomiasis in children. In patients suspected clinically of having the disease stool ex-

amination may be performed and, if negative, a complement-fixation test and skin test on the back should be made. If one of the immunological tests is positive, stool examination should be repeated up to four times and if still negative rectal biopsy should be performed. In epidemiological surveys complement-fixation tests and stool examinations give equally satisfactory results, but the complement-fixation test has certain practical advantages. The results of the skin tests in epidemiological surveys should be interpreted with caution.

CANADA

Canada's Health.—At the joint meeting of the British and Canadian Medical Associations Dr. Gordon Wride (Ottawa) gave an account of the Canadian national sickness survey. At the time of the survey each person had in one year approximately one disability period due to illness, lasting on an average 12 days. Of those suffering from illness 75% did not stop their usual activities. Days confined to bed averaged 5.6 per person.

Over 75% of those reporting sickness had new illnesses during the survey period, the incidence being highest in children. The highest incidence of illness occurred in those under 15 years of age, and the lowest in those aged 15 to 24. After this age the period of sickness tended to increase steadily with age. Women had slightly more illness than men (60.7% of all women compared with 56.2% of all men), and 52% of all women required some period of treatment in bed, compared with 44.1% of men. These differences could be partly explained by the incapacity of young adult women in the childbearing age. The common cold and influenza caused more absenteeism than all other illnesses. After these were gastric complaints, acute pharyngitis, and conditions with symptoms in the back and limbs. Respiratory disease was common in children, more than 75% being affected in the survey period. After this in order of frequency were infective and parasitic diseases.

The diseases affecting the group aged 45 to 65 years were mainly those affecting the bones, limbs, and circulatory system. The survey showed that 80% of the population had some illness in the course of a year and that in this time each person affected has an average of 2.5 bouts of illness. Just over 50% of the population reported some medical care by physicians. Of this 43% was given by general practitioners, and 10% of all patients had inpatient treatment. More than 40% of the population received calls from physicians or made office visits. The physician was consulted in 25% of all cases of illness. House calls were made mainly for those under 15 and those over 65 years of age. The average number of physicians' calls or visits per 1,000 population was 1,786 or 1.8 per person per year. The average number of days per person spent in the hospital increased with age.

The 4,555,000 family units making up Canada's population spent $373,800,000 on health services in the survey period. Direct payment to physicians was made by 23.5% of the population and indirect payment through prepayment plans by 3.2%. The survey revealed that one million Canadians have a permanent disability of some sort; 414,000 are severely disabled; and 90,000 "totally" disabled, but 33% of the "totally" disabled are at work. In order of frequency the disabilities were due to heart and arterial disease, accidents, arthritis and rheumatism, disorders of the nervous system, deafness, and blindness.

FINLAND

Deaths from Parathion.—Parathion, first used as an insecticide in World War II, is now being used in increasing quantities. Due to its anticholinesterase action and the resulting rise in acetylcholine concentration it stimulates the parasympathetic nervous system and peripheral nerve endings. Exposure to high concentrations, which may enter the body through the respiratory tract or skin, can cause death within a few minutes, although the usual period is one-half-to-four hours. Toivonen and coworkers in Helsinki reported the increasing frequency of parathion poisoning (*Lancet* 2:175, 1959). Between 1952 and 1957 there were 286 deaths in this country due to parathion pesticides. In the last year for which figures are available there were 105 deaths. Of the total number of deaths only 17% were accidental, the remainder being suicidal. The number of suicides in Finland from taking parathion is greater than that from hypnotics and barbiturates. The latter are responsible for about 40% of the total number of suicides. Most of the accidental deaths were in small children given a parathion mixture in mistake for medicines, such as cough mixtures. In adult accidents a parathion mixture was frequently taken inadvertently in a period of alcoholic intoxication. In 20% of the deaths the victim had access to parathion in the course of his or her work. The remaining 80% seem to have had little difficulty in buying or acquiring the poison.

FRANCE

Ureteral Calculi.—J. and E. Thomas and co-workers at the meeting of the National Academy of Medicine on April 7 reported that neither a solution of lithium salts nor a solution of urea were found to be capable of dissolving uric acid calculi in situ. On the other hand, a solution of piperazine did dissolve such calculi. Since piperazine is a strong

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base it is necessary to bring the pH of this solution to 8 or 9 when it is used for urologic purposes. This can be accomplished by adding phosphoric acid. Under these conditions a solution of piperazine containing 17.8 Gm. per liter dissolved 5 Gm. of uric acid per liter at a temperature of 20 C. To avoid disturbances connected with resorption a solution of piperazine of 5 Gm. per liter was recommended. This was given by intraureteral perfusion for a few hours daily. Too long a perfusion period may result in an undesirable piperazine resorption.

Cigarette Filters.—At the meeting of the same Academy on May 12, J. Paraf and co-workers reported on the use of a filter which they perfected. It consists of cotton impregnated with polymerized furfural. The study was made in heavy smokers who had no organic lesions in the respiratory tract. A series of 76 persons smoked cigarettes with common commercial filters, and 61 smoked with furfuralized cotton filters. In the first group the undesirable respiratory and other side-effects were reduced by about 22% of the intensity observed when cigarettes with no filters were smoked, but in those who used furfural filters the average reduction was 50%. Here it must be added that in 25% of the subjects side-effects were completely or almost completely eliminated. Laryngeal, tracheal, and bronchial irritation and nausea and anorexia disappeared. It is important that the smoker retain the taste of the smoke because when this is masked or weakened, the smoker inhales more vigorously and this diminishes the effectiveness of the filter. Also by increasing the temperature of the smoke passing through the filter the production of noxious elements is increased. The authors believed that no other filter so effectively retains tars and nicotine without diminishing the aromatic qualities of the smoke as does theirs.

Late Results of Operation for Gallstones.—At the meeting of the Academy of Surgery on May 20, B. Kourias and A. Tobler reported on a series of 550 patients who had been operated on for gallstones between 1950 and 1955. The results were excellent in 70.4% of the patients. There were no symptoms even in those who committed dietary excesses. In 17.4% mild symptoms occurred after dietary indiscretion. In 6.5% of the patients some improvement was observed but they still had occasional attacks of pain. Relapses or operative failures were noted in 5.7%. Operative failures were due to stones overlooked in the principal biliary passages, biliary dystonia, colitis, or hydronephrosis. The mild symptoms present in some were believed to be due to transient dystonia of the biliary duct because of ablation of the gallbladder, chronic pancreatitis, or hepatitis. The excellent results were attributed by the authors to the preoperative use of cholangiography.

Psychic Disturbances due to Isoniazid.—A. Lepeuple and co-workers (*Revue de Tuberculose et de Pneumonologie*, no. 3, 1959) studied a series of 621 tuberculous students of about the same age and mental level, who were treated with isoniazid. Such psychic disturbances as discreet hypomania, mania, manic-depressive psychosis, and confused dream-like states are frequently produced by this drug. Previous psychic disturbances existed in 7% of the 621 students. Severe psychosis and neurosis was found in 4.6% of them. These factors must be taken into account in interpreting the disturbances occurring following the use of isoniazid. Thus, among the patients who had no history of psychic disorder, only 1.56% manifested such disturbances, as compared with the occurrence of these disorders in 33% of those who had had previous psychic disorders. On the other hand, the daily dose had no clearly defined influence on the occurrence of these disorders. The blood level of free isoniazid, which is not always in proportion to the absorbed dose, plays an important role. The patients who manifest psychic disorders with a low isoniazid level are those who were previously the most severely disturbed. It is possible that there is a threshold of toxicity in each person beyond which psychiatric complications may occur. This threshold is lower in persons with a history of previous psychic disorders.

Paralysis Agitans.—P. Morin (*Revue Médicale Normande*, no. 1, 1959) studied a series of 100 patients with paralysis agitans who were operated on by pallidolenticular coagulation. The operation was performed with the patient (previously subjected to trepanation) conscious and consisted of local electrocoagulation. The author observed two severe complications; one patient had a fatal hemorrhage and the other became confused, but he recovered completely within two months. In 75% of the patients the tremor and rigidity disappeared either immediately after electrocoagulation or within a few weeks. A certain number of patients had a mild relapse. This operation had, on the other hand, a variable effect on walking and on general motility. In some patients there was a marked improvement and in others none at all. Speech, facies, and hypersialorrhea were not improved and sometimes were aggravated. The best results were obtained in young patients whose disease was predominantly unilateral and of short duration.

Cobalt and Penicillin.—C. H. Chouard (*Revue de Pathologie Générale et de Physiologie Clinique*, 1959) emphasized the quantitative and qualitative increase in the effectiveness of penicillin when given with cobalt acetate. A series of 24 patients who had acute exudative otitis and other otolaryngologic infections was treated with this combination. The results were favorable in all. Three patients with acute exudative otitis were cured

without paracentesis within two to six days. Six patients with otitis, in which the protracted course suggested mastoiditis and who were subjected to paracentesis, were completely cured within a fortnight. Of five patients with suppurative adenitis of the neck, three were cured without any other therapy. One patient with nasopharyngitis was cured within a few days. The condition of two patients with nasopharyngitis associated with otitis was improved within one week. Some authors believe that cobalt leads to a diminution of the oxygen consumption by the bacteria. Others suggest that cobalt increases phagocytosis. Cobalt works synergically with no other antibiotic than penicillin.

GERMANY

Resection of the Thoracic Section of Esophagus.—H. Manseck (*Zentralbl. Chir.* 83:301, 1958) stated that even when treatment of intrathoracic pressure made possible resection of the thoracic portion of the esophagus, this operation was justified only in patients with malignant tumors. Advances in surgery in the last 10 years have helped to reduce the danger in such an operation. These advances include the introduction of antibiotics, the management of pressure difference on opening the thorax, and perfection of a technique for using the stomach as a substitute for the esophagus. Potentiated curare narcosis, after use of high-pressure narcosis with intubation, has been of great value. The author reports on two patients on whom a transthoracic operation, without opening the abdomen, was performed. One patient had a resection of the cardia because of suspected malignancy with stenosis and the other had an epiphrenal diverticulum that had caused marked dilatation of the esophagus. Both patients were cured. Benign tumors of the esophagus usually do not require resection. They can be removed by endoscopy, like papillomas or mucosal polyps. Manseck avoids wide opening of the abdomen and thus greatly reduces the operative trauma.

Asbestosis.—Hertz and Reinwein (*Ärztl. Wchnschr.* 14:361, 1959) reported on three patients who had worked with asbestos insulation for 10, 21, and 23 years. They were admitted because of chronic bronchitis refractory to treatment. All had the subjective symptoms of pulmonary fibrosis: cough with tenacious sputum, stabbing and dull pains in the thorax, and dyspnea. The sputum in all three contained asbestos bodies, which could be demonstrated by adding to the sputum an equal amount of Antiformin (sodium hypochlorite), centrifuging, and examining the deposit microscopically. Typical radiologic changes of the lung consisting of strand-like shadows and cloudy turbidities in the lower lobes were present in only one patient. There is often a significant discrepancy in asbestosis between clinical and roentgenographic findings. Pulmonary changes demonstrable by radiology are usually much more unobtrusive than in silicosis. Asbestosis cannot, therefore, be diagnosed by x-ray examination alone, since this method reveals mainly alterations of the substrate, but not the primary functional disorders that constitute the first clinical symptoms.

Testing of pulmonary function showed that, according to the degree of pulmonary fibrosis present, vital capacity was reduced in all three patients as the result of a restrictive disturbance of ventilation. Expansion capacity of the lung was diminished due to increased rigidity of the tissue and, therefore, elastic resistance was increased. One patient had an obstructive ventilatory disturbance also. Disturbances of pulmonary function were generally greater than might be thought from the roentgenograms. Puncture for a sanguinolent pleural effusion was made in one patient. Although the effusion did not contain tumor cells, an asbestos carcinoma, which is found in about 20% of cases, was suspected. Asbestosis should be recognized as an occupational disease. Since management of the disease, as of all other pneumoconioses, is confined to purely symptomatic treatment, preventive measures are of great importance. If impairment of pulmonary function is already manifest, it is imperative to remove the patient from the hazardous surroundings in order not to aggravate the unfavorable prognosis of asbestosis by further exposure.

Penicillin-resistant Gonococci?—H. Röckl (*München, med. Wchnschr.* 101:708, 1959) stated that penicillin-resistant gonococci have not emerged after more than 10 years of treating gonorrhea with penicillin. The so-called penicillin failures are attributable to diagnostic mistakes (confusion with pseudogonococcic strains); reinfection; and insufficient penicillin dosage or local conditions preventing an adequate antibiotic level at the site of infection. The question whether the penicillin sensitivity of gonococcic strains has decreased in the course of the years was investigated by means of gonococcic cultures; 52 strains were tested in the first half of 1956, and 51 strains two and one-half years later. The strains were selected at random from patients with gonorrhea.

The collective mean of total growth inhibition was 0.0058 U. per milliliter in 1956 and 0.0150 U. per milliliter in 1958, which shows a marked increase. While a penicillin concentration of 0.01 U. per milliliter effected total inhibition in 57% of all strains in 1956, the corresponding figure for 1958 was only 23%. The highest limit of growth (0.1 U. per milliliter in 1956) was surpassed in 1958 by three collective strains. These results show a significant decline of penicillin sensitivity of gonococci, which is ascribed mainly to a gradual adjustment of gonococci to penicillin in the course of the

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years, besides the factor of selection (eradication of sensitive strains). Complete resistance has not, however, developed.

Cardiac Decompensation.—In cardiac therapy digoxin is of special importance. Because its action is intermediate between the fleeting action of strophanthin and the sustained retention of digitoxin, it offers great advantages in general practice. In combination with oxyethyltheophylline and nucleosides it affords a convenient means of treatment. P. Könner (*Medizinische* 11:489, 1959) used such a composite preparation, Parmanil-digoxin, to treat a series of 65 patients. The preparation was well tolerated and the author pointed out the improved glycoside tolerance, increased diuretic effect, and improvement of cerebral and coronary circulation resulting from its use. The latter property is important because cardiac decompensation is associated with coronary insufficiency in most patients. The drug is suited for the treatment of all types of cardiac insufficiency, including the specially glycoside-sensitive forms.

The guide for dosage is the pulse rate which usually returns to normal within five to seven days. In 50% of the patients treatment was initiated with intravenous injections, giving one ampul two times daily for about five days. Thereafter treatment was changed to tablets. The other group received the preparation orally from the start: 3 tablets daily were required until saturation was achieved in four or five days; for maintenance usually 2 tablets daily were required. The rapid onset of dehydration (diuresis) in most patients rendered additional diuretic medication superfluous and prevented the passage of glycoside into the congestion fluid, thus, precluding incalculable redigitalization.

Ionizing Radiation of Cutaneous Cancer.—C. G. Schirren of the University of Munich (*München. med. Wchnschr.* 101:1269, 1959) evaluated various methods in the management of cutaneous cancer by means of ionizing radiation. These included contact irradiation; soft-ray irradiation by means of the beryllium tube; y-rays originating from the series of natural (radium) and artificial (cobalt) radioactive substances; beta-radiation with strontium, yttrium, and phosphorus; and the electron accelerator. Those methods are theoretically preferable which deliver the largest possible concentration of the dose to the tumor. From this standpoint the electron accelerator is the method of choice. Due to extremely high purchase and maintenance costs, however, it cannot be generally used. Apart from special cases, y-radiation produced no better therapeutic results than contact and soft-ray irradiation. Their application, however, is more complicated and is associated with a stronger genetic stress. Beta rays possess a limited range of indication, as they can be used only to treat flat tumors. Among the methods of ionizing radiation, radiotherapy is still of greatest significance for practice. In the therapy of cutaneous cancers soft radiation is now replacing contact radiation.

Death of Prof. Adolf Windaus.—According to a report in the *Deutsche medizinische Wochenschrift* of Aug. 21 Adolf Windaus, emeritus professor of chemistry and former director of the Chemical Laboratories of the University of Göttingen, Germany, died recently at 82 years of age. He was an outstanding biochemist who made important contributions, particularly to the study of vitamin D and its use in the prophylaxis and treatment of rickets. In 1928 the Nobel prize in chemistry was awarded to him for his studies on the nature of sterols and their connections with vitamins. Later studies in his laboratory contributed to the investigation of a chain of ergosterols, such as lumisterol, tachysterol, calciferol (vitamin D_2), activated 7-dihydrocholesterol (vitamin D_3), suprasterol, and dihydrotachysterol.

INDIA

Chlorpromazine for Tetanus Neonatorum.—Nazareth and Edibam (*Indian Journal of Child Health*, vol. 8, July, 1959) achieved a significant reduction in the mortality of tetanus neonatorum with the use of chlorpromazine. The usual treatment with sedatives, antibiotics, and antitetanic serum had resulted in a death rate of about 88%, but with a combination of chlorpromazine, antitetanic serum, and procaine penicillin this was reduced to 56%. The authors treated a series of 16 patients who had tetanus neonatorum with this combination. All of these infants were delivered at home by an unqualified midwife or a relative without any aseptic precautions. The age of the infants on admission was between 5 and 21 days. In 12 patients with an incubation period of seven days or less, only 4 survived. Of four with an incubation period of eight days or more, three survived. Survival in the patients with a short incubation period was attributed to the use of chlorpromazine. The period of onset is also important in the prognosis. There is a greater chance of survival when this period is longer than 24 hours. Of eight patients whose period of onset was less than 24 hours, only one survived but of the remaining eight with a longer period of onset six survived.

The first sign of the disease was failure to nurse. This was followed by stiffness of the back and spasms. The umbilicus was sodden or moist in all except one who had gross umbilical sepsis. A positive gag reflex was an important diagnostic sign, generalized spasms being induced by attempts to open the mouth. Eleven had severe and five had mild spasms. All in the latter group and only two in the former survived. Fever lasting for more than

48 hours after admission was a bad prognostic sign. Two infants who were afebrile throughout survived but another had severe spasms and died 40 hours after admission.

Treatment was carried out in a separate darkened room, feeding being left to nurses. Locally only simple dressings were used for the umbilicus. Treatment consisted of administration of procaine penicillin and aspirin. Tetracycline was given to three patients but was of no help. Prednisolone was given to two patients to control fever but was also of no help. For sedation, chlorpromazine was used in a total daily dosage of 14.3 mg. per kilogram of body weight. Excellent sedation was obtained in patients with moderately severe spasms. Of six such patients, only one died. Sedation lasted for one to two hours and the babies went to sleep about 20 minutes after injection. They could be aroused for a feeding and slept immediately afterward. Although spasms recurred in two hours, they were much reduced in frequency. In patients with severe spasms chlorpromazine alone did not help and secobarbital per rectum used in addition controlled the spasms for four or five hours. In seven patients spasms could not be controlled even with both of these drugs. These had had a short onset and all of them died. No toxic effects were observed with the use of chlorpromazine in this dosage. The injections could be given at six-or-eight-hour intervals and even slightly larger doses than those used here might be used to control the spasms more effectively. The drug was given till the baby started taking oral feedings. Usually it had to be given for about 10 days after admission.

The authors got better results with chlorpromazine in childhood tetanus than in tetanus neonatorum but even in the latter its use led to an increase in recovery rate. Tube feeding was started on admission and the tube could be passed more easily 15 to 30 minutes after injection of chlorpromazine. It was changed every 24 hours. Tube feeding, however, carries the risk of inhalation of regurgitated milk and three patients in this series died of this complication. Oral feedings could be started by about the seventh or eighth day. Subcutaneous infusion was used in only one patient and he died. The authors recommended avoidance of any infusions during the first eight days. No operations such as tracheotomy or umbilectomy were performed on any of the patients. The usual dose of antitetanic serum was 30,000 units. This comparatively small dose was found to have certain advantages. Thus, the initial temperature after the administration of the serum returned to normal much earlier and remained so. A secondary rise sometimes occurred on the fourth to seventh day but this was also mild. The smallness of the dose did not influence the cure rate adversely. The total quantity of serum injected being much less, there was less pain at the site of injection and the chances of abscess formation were also similarly reduced. Economically it is of great advantage.

Tranquilizers.—F. N. Shroff and co-workers (*Journal of J. J. Group of Hospitals and Grant Medical College*, vol. 4, July, 1959) assessed the tranquilizing effects of chlorpromazine, reserpine, meprobamate, and an indigenous drug known as malakanguni in an experimental study. In one group of experiments, the effect of these drugs on convulsions produced by epinephrine, pentylenetetrazole, picrotoxin, and strychnine was observed. The dose of the convulsant was such as to produce 100% mortality in 10 rats. Tranquilizers were injected either before or simultaneously with the LD_{100} of the convulsant drug. The behavior pattern of albino rats was studied after a single dose of these drugs and the sedative effect noted. Their effect on pentobarbital anesthesia was observed by first injecting the pentobarbital intraperitoneally in mice and noting the onset of sleep and righting reflex time. The drug to be tested was then given simultaneously or one hour before the barbiturate injection and alterations, if any were noted.

The antispasmodic effect of these drugs was studied on isolated guinea pig ileum and rabbit duodenum preparations. Contractions were induced with acetyl choline or histamine. The drugs to be tested were injected in the bath three minutes prior to injection of acetyl choline or histamine and the effect on contractions noticed. Of the convulsants used in rats, epinephrine caused marked excitement and 60% mortality in the dosage used, while with the other convulsants there was 100% mortality. None of the tranquilizers could counteract the effect of epinephrine. Meprobamate, chlorpromazine, and reserpine actually led to an increase in the mortality induced by this drug. Meprobamate was remarkably effective in convulsions induced by pentylenetetrazole, producing a 100% reduction in mortality. Malakanguni lowered the mortality by 60%. Chlorpromazine and reserpine had no effect on these convulsions. Meprobamate reduced the mortality after picrotoxin convulsions by 40%, reserpine by 100%, malakanguni by 20%, and chlorpromazine was ineffective.

This difference in action of the tranquilizers may be related to their different sites of action. Meprobamate antagonized strychnine completely while the other drugs did not show much effect. Malakanguni and reserpine actually enhanced the effects of strychnine. The righting reflex time was increased by reserpine, malakanguni, and chlorpromazine. All except meprobamate had a potentiating effect on the sedative action of pentobarbital. The reduction in mortality was not significant with any of the drugs. As an antispasmodic, meprobamate was ineffective, malakanguni caused 50% reduction, and chlorpromazine and reserpine showed

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some antispasmodic action. Meprobamate was unique in its action against strychnine, which was not shared by other tranquilizers. From the different effects observed, these drugs have been divided into autonomic suppressants and central relaxants. The relaxants would be primarily helpful in the treatment of psychoneuroses and the autonomic suppressants could be helpful for treatment of psychoses. The indigenous drug, malakanguni, was noted to have all the properties of a tranquilizer.

Hypertension.—M. J. Pandit studied the incidence of hypertension in 1,978 men and 1,267 women attending the J. J. Hospital, Bombay (*Journal of J. J. Group of Hospitals and Grant Medical College*, vol. 4, July, 1959). The patient was considered to be hypertensive if the basal reading (readings were taken at 5-minute intervals after the patient had been lying down for 15 to 20 minutes, till a constant reading was obtained), was persistently high (160 mm. Hg or over for the systolic and 100 mm. Hg or over for the diastolic pressure). In the author's series 65 patients were found to be hypertensive, giving an incidence of 2%. The incidence was slightly higher in women than in men. No positive family history of hypertension was obtained from any patient. Body build was determined in 30 hypertensive patients, 6 were stout, 19 average, and 5 thin. Most of these patients belonged to the poor working class and indulged in an active occupation. Psychological factors were probably partly responsible in 5 of the 30. Eight patients had secondary hypertension, five of renal origin, and all were below 40 years of age; the remaining 22 had primary hypertension and were 40 years of age or over. In 28 the hypertension was benign and in 2 it was malignant. Giddiness, dyspnea, and headache were the most common symptoms.

Venereal Diseases.—Tampi and Rao (*Indian J. Dermat. & Venereal.* **25**:2 [April-June] 1959) analyzed the source of infection in 1,358 patients (1,248 men and 110 women) attending the venereal disease clinic between 1954 and 1959. Of these patients 227 were not sure about the source; 257 had primary syphilis, 207 secondary syphilis, 270 gonorrhea, and 624 chancroid. Of the women, 88 acquired the infection from their husbands, while 170 men got the infection from their wives. Of the remaining 873 for whom the source of infection was known, in 418 or 47.9% it was acquired from prostitutes.

Encephalitis in Children.—Manchanda and Gupta (*Indian Journal of Child Health*, vol. 8, July, 1959) studied 45 children who had a diagnosis of encephalitis in the summer of 1958. The criteria for diagnosis were an acute onset with fever, involvement of the central nervous system after a variable prodromal period, and drowsiness or coma. Convulsions, if present, were followed by unconsciousness usually for more than 24 hours. The spinal fluid showed bacteriologically negative findings and a normal or elevated cell count. These cases occurred between July and October. The youngest patient was 8 months old and the oldest was 11 years of age. In only five was there a history of similar disease in another member of the family or in the immediate neighborhood.

The clinical findings conformed to one of four types: (1) acute fulminating onset with vomiting, chills, and a temperature of 107 to 109 F; (2) acute infection with cerebral involvement, with rigidity, convulsions, and drowsiness or coma; (3) acute gastroenteritis with vomiting and diarrhea leading to severe dehydration and circulatory failure within 24 hours; and (4) insidious onset but after a variable period, with evidence of one of the above patterns. Treatment essentially consisted of hydration, resuscitation, hydrotherapy, sedation, and antibiotic therapy, the latter including parenterally administered crystalline penicillin, streptomycin, and broad-spectrum antibiotics. An acute onset with chills, gastrointestinal symptoms, high temperature, coma, and convulsions was associated with a bad prognosis. No form of treatment seemed to influence the prognosis. Follow-up revealed the presence of left-sided hemiplegia in two patients and mental changes in two. In this epidemic 26 patients died.

Dermatomycoses.—R. N. Gupta (*J. Indian M. A.* **33**:2 [July 16] 1959) analyzed a series of 620 patients with dermatomycoses and found that Trichophyton rubrum was the most prevalent species responsible for this disease. T. rubrum caused 56.73%, T. mentagrophytes 31.73%, Epidermophyton floccosum 1.92%, and other organisms 9.62%. Although all parts of the body may be affected, the groins and genitals followed by hands, feet, face, scalp, and nails were most commonly involved, and the men outnumbered women 3:1. Adults accounted for 60.32% of the cases, persons 12 to 20 years old for 33.23%, and younger children for 6.45%.

UNITED KINGDOM

Nurses' Examinations.—In a letter to the *Lancet*, Drs. Walther and Raeburn criticized the questions asked nurses in their final examinations. A typical examination included the following questions: discuss symptoms, signs, complications, treatment, and prevention of rheumatic fever; give causes, management, and treatment of prolonged loss of consciousness; give brief accounts of tetany, hay fever, polyuria, polycythemia, and myxedema; and state the uses, doses, and dangers of streptomycin, meperidine, paraldehyde, and vitamin B_{12}. Accord-

ing to the writers such questions might reasonably be asked doctors in a qualifying examination, but not nurses. They do not ensure that a good nurse shall pass and a bad one fail. Should a nurse have to diagnose, treat, and prevent rheumatic fever, or correct a doctor's dose of certain drugs? These questions do not test nursing ability. If nurses have to know as much as doctors in addition to being nurses, then they should be paid in proportion. The writers suggest that such difficult questions are asked because they are easier to mark. They blame the doctors who prepare the questions and the General Nursing Council for permitting them. Since it is hard enough to recruit girls for a career in nursing, it is the height of folly to frighten prospective candidates away with such examination questions as those quoted.

Quinine Oxidase and Liver Disease.—It is known that an enzyme in the liver oxidizes quinine, being specific for the oxidation of the pyridine nucleus, which is present in quinine and nicotinic acid. Roman and Dulmanis believed that the estimation of this quinine oxidase in serum is an easy and reliable biochemical test for parenchymatous liver damage, since this enzyme is derived only from the liver (*Lancet* 2:90, 1959). They estimated the enzyme level by determining the amount of quinine oxidized by spectrophotometry, the oxidation product having an increased optical density. This is determined after incubating a weak solution of quinine with the serum under test. One unit of quinine oxidase is that amount which causes an increase in optical density by 0.001 under the conditions specified. In normal subjects and in diseases in which the liver is not involved there were less than 5 units of quinine oxidase per milliliter of serum.

In 48 patients with infectious hepatitis the quinine oxidase level varied from 7 to 89 units. In a patient with toxic hepatitis it was 25 units, dropping to 12 units a week after clinical improvement. In general, the milder the clinical symptoms the lower the level of quinine oxidase. Of 20 patients with hepatic cirrhosis raised values were found in three, while those in all the others were below 5 units. The authors believed that this test is of value not only in differentiating between toxic or viral hepatitis and obstructive jaundice but also in the diagnosis of infectious hepatitis in patients with general malaise, and as an indication of active parenchymatous liver damage when other tests are inconclusive.

Hypertension After Gestoses.—In spite of extensive literature there is still some difference of opinion on whether permanent and significant hypertension is a frequent sequel to toxemias of pregnancy in women with a normal blood pressure who become pregnant, and on the amount of damage done by toxemia in a woman who is already hypertensive. Gibson and Platt made a four-year follow-up study of 446 patients who had pre-eclamptic toxemia and whose blood pressure early in pregnancy was normal (*Brit. M. J.* 2:159, 1959). They took the figure of 140/90 mm. Hg as an arbitrary dividing line between normal blood pressure and hypertension during or before the 20th week of pregnancy. From an analysis of the data there seems little doubt that gestoses cause a permanent increase in blood pressure beyond that which can be explained by the passage of years. This was shown by comparison of the blood pressures with those of healthy controls of the same age and sex. Individual differences existed and a number of women with a history of a gestosis showed no permanent rise of blood pressure. Rarely was the rise in blood pressure of an initially normotensive woman sufficient to seriously affect the expectation of life. Only 17 of the 446 women, or just under 4%, were left with a diastolic pressure of over 105 mm. Hg.

A series of 92 women in whom toxemia of pregnancy was superimposed on hypertension was also followed up. The same criteria employed formerly were used. This group also had a rise in blood pressure four to five years later that was higher than could be accounted for by an increase in age alone. There were, however, extreme variations from person to person, and there was little correlation between the height of the starting blood pressure and the ultimate increase in pressure.

Electrocardiograms in Symptomless Men.—Much reliance is placed on the electrocardiogram (ECG) in the diagnosis of cardiac ischemia, particularly when the pain is atypical. In fact, chest pain with an abnormal ECG is often regarded as cardiac in origin. To assess the reliability of the ECG in diagnosis it is necessary to know how often an ischemic tracing is a chance finding in subjects without cardiac disease. Weitzman and Smith investigated the incidence of coronary ischemia in men without chest pain in the group aged 50 to 80 years. This is the group in which the incidence of coronary artery disease is greatest (*Brit. M. J.* 2:162, 1959). Rigorous criteria to exclude other causes of electrocardiographic abnormality were adopted. The subjects studied were 100 male hospitalized patients who had no history of chest or shoulder pain or any type of heart disease and no cardiac enlargement, diabetes, renal disease, syphilis, peripheral or cerebral vascular disease, or arrhythmia. All had a serum cholesterol level under 300 mg. per 100 ml. and a diastolic blood pressure below 90 mm. Hg. A 12-lead ECG (I, II, III, AVR, AVL, AVF, and V_{1-6}) was recorded at rest, and leads V_5 and V_6 were repeated at 2-minute intervals for 10 minutes after exercise unless the subject was not fit for it.

The usual criteria for electrocardiographic evidence of myocardial ischemia were used, namely large Q waves, flattening or inversion of T waves, and depression of the S-T segment at rest or after exercise. Although such S-T and T wave changes are not specific and can be produced by other cardiac conditions and electrolyte disturbances, patients with these changes were excluded. Flattening of T waves alone or S-T depression of less than 1 mm. was not accepted as evidence of cardiac ischemia unless square depression of the S-T segment of greater amplitude followed exercise. Twelve of the 100 ECGs were suggestive of myocardial ischemia, although there was no other evidence of heart disease. Autopsy was performed on 19 patients and 6 of these had had electrocardiographic evidence of ischemia during life. None of them, however, had evidence of coronary disease when the arteries were injected post mortem with bismuth oxychloride and examined radiologically. These findings emphasize the need for care in relying solely on electrocardiography for the diagnosis of chest pain, which may not be necessarily of cardiac origin even if the tracing is abnormal.

In 59 of these men, including 9 with abnormal ECGs, the serum lipoproteins were examined by paper electrophoresis for the presence of an abnormal pre-beta-lipid band, which is stated by many workers to be associated with myocardial infarction. A moderate pre-beta-lipid band was found in 50% and a large pre-beta-band was found in 10% of the patients with no pain and normal ECGs and in healthy men. A large pre-beta-lipid band was observed in 33% of the patients with electrocardiographic evidence of myocardial ischemia, with or without symptoms, but it was also seen in patients with a number of unrelated conditions. Weitzman and Smith believed that where there was marked metabolic disturbance the lipoprotein patterns might also be disturbed, and this must be borne in mind. The lipoproteins are not specific indicators of coronary disease.

Health Service Report.—The Ministry of Health has issued its report on the National Health Service (NHS) for 1958 (Report of the Ministry of Health for the Year Ending December 31, 1958, part 1, 1959, London, Her Majesty's Stationery Office). The total cost of the NHS in England and Wales for the fiscal year ending March 31, 1958, was 1.76 billion dollars, 75% of which was paid by the exchequer. This is an increase of 115 million dollars over the previous year. The balance was paid for out of local taxation, health service charges to patients, superannuation contributions, and payments from compulsory NHS contributions, which were increased just over a year earlier. Slightly more of the cost of the service is now borne by the direct contributions of people of working age. The cost of hospital and specialist services increased in 1958 by 64.5 million to 950 million dollars. This was partly due to the rise in the prices of goods and services, which increased by 3.5%. Wage increases accounted for 28 million dollars. There was increased use of the hospital service. There were 3,889,000 inpatient treatments, an increase of 95,000 over the previous year, without an increase in the actual number of beds. Waiting lists were 443,000, which was about the same as in 1957. Hospital beds were allocated to the various specialties in the following percentages: mental conditions, 44.3; surgical, 14.8; medical, 14.7; chronic sick and geriatric, 12; obstetric, 3.7; general practitioner units, 2.1; gynecologic, 2; convalescent, 1.6; and miscellaneous 4.8. Private patients occupied 1.2% of all hospital beds. In 1958 the average weekly cost of caring for an inpatient with an acute condition in a London teaching hospital was $93 and in the provinces $75. The average cost throughout the country in nonteaching hospitals was $33.33.

The number of general practitioners working as principals increased from 19,343 to 19,599, and 13,253 were in partnership, or 291 more than in 1957. The average number of patients per doctor was 2,267, which was about the same as in 1957. The number of prescriptions dispensed by pharmacists fell by 4 million, but their cost, which was 184 million dollars was 11.6 million dollars more than in 1957. This was attributed to an increase in the average prescription cost of 75 cents to 90 cents and to the introduction of newer and more expensive drugs. The more expensive antibiotics and steroids made up 34% of all drugs dispensed by pharmacists. The reduced number of prescriptions for the year was explained by the absence of any major epidemics and by the imposition of a prescription charge on all patients. More women had their confinements at home in 1958. The number of domiciliary confinements attended by midwives was 265,215. This was 9,468 more than in 1957. Doctors were present at only 44,964 of these, although they were engaged to attend 220,823.

Less than half (44.5%) of the babies under one year of age received primary vaccination against smallpox. At the end of 1958, 46.7% of the children under 15 years of age had been immunized against diphtheria and 470,290 against whooping cough. By the end of the year about 6 million children aged 15 or under had received two injections of poliomyelitis vaccine. This represents 60% of all children in this age group. The response to free vaccination against poliomyelitis by those in the age group 16 to 25 and by expectant mothers was disappointing. In his comments on the use of the health service the Minister of Health stated that the public is too preoccupied with disease, drugs, and hospitals. The country and the in-

dividual would gain if people thought more of preserving good health and acted on the advice given them on how this can be achieved.

Menière's Syndrome.—A new operation performed by Dr. R. B. Lumsden of the Edinburgh Royal Infirmary for the relief of Menière's syndrome was televised at the joint BMA-CMA Meeting at Edinburgh. The object was to destroy the function of the semicircular canals by ultrasonic vibrations without impairing hearing. The canals were exposed by chipping away the mastoid bone. Electric vibrations of about one million cycles per second were converted into ultrasonic vibrations by a special crystal of quartz and directed as a fine beam on the semicircular canals for about 30 minutes. This destroyed the epithelium lining the canals, inactivated the labyrinth, and relieved the vertigo, but did not impair hearing, although over-exposure can permanently damage the seventh cranial nerve.

Lumsden offers operation only to those patients who have failed to benefit from medical treatment and are physically and socially handicapped by their disease. The operation is performed under local anesthesia and the patient is made drowsy with an intravenous injection of meperidine. It is essential that the patient remain conscious as the seventh cranial nerve is tested by asking him from time to time to contract the facial muscles. So far 22 patients have been operated on by this method with complete relief in 13 and improvement in 4. A deterioration of hearing to the extent of 10 to 20 db. occurred in five patients. Histological studies on cats showed that exposure to ultrasonic vibrations caused degeneration of the neuroepithelium of the semicircular canals, but in the dosage used to cause this the organ of Corti was left intact.

Cancer Education.—The first traveling unit in Britain for giving information on cancer recognition and treatment is being launched by the Manchester Committee on Cancer. It will visit factories, offices, stores, and workshops. A specially trained nurse will travel with the van, which is equipped with cine-projector, collapsible screen, films, and literature. The nurse will give talks and show films to groups of workers and answer their questions. Such a program should have economic advantages for industrial and commercial firms. Every trained worker who seeks advice too late for curable forms of cancer represents a needless loss of skill and man-hours.

The committee is an independent voluntary body. Its educational project, started in 1951, now serves 2,500,000 people. The annual report on the project says that a public opinion poll showed a notable improvement in the number of women who believed that cancer could be cured, 55% at present as against 36% in 1953. The number of those who thought early treatment increased the chance of cure had risen from 57% to 71%. There was no comparable improvement in towns not included in the educational project.

Pharmacists Warned of the Danger of Escapist Drugs.—The Council of the Pharmaceutical Society of Great Britain issued a statement to pharmacists warning them of the dangers of the indiscriminate use of escapist drugs acting on the central nervous system. Many of these are obtainable in the drug store without a doctor's prescription and are not subject to legal control. The council warned that drugs that stimulate or depress the central nervous system might lead to habit formation or even to addiction in some patients. Tolerance is rapidly developing to many such drugs, so that they are taken in increasing doses which might lead to changes in character and behavior detrimental to both the patient and society. Some time lag between the introduction of new drugs and the control of their sale by legislation is probably inevitable, but the council believes that, in general, drugs stimulating or depressing the central nervous system should not be supplied on request to the public.

A knowledge of the use of drugs dealing with conditions of stress or taken for their euphoric effects is widespread among the public, owing to modern advertising, and pharmacists are often under pressure to supply such drugs to patients who are not taking them under medical supervision. The council stated that this could only bring discredit to pharmacists, if by the indiscriminate sale of such drugs they encouraged the belief that the stresses of life could be escaped or evaded by the use of drugs instead of being faced and surmounted. A list of 29 drugs that were not, but should be, subject to legal control was issued by the council.

Inoculation Recording by Tattooing.—Norman Lake of Charing Cross Hospital (*British Medical Journal*, Aug. 8, 1959) stated that with an increase in immunization programs the need for some method of indelibly recording the protection in a readily available manner is receiving much attention. In the case of tetanus inoculations, it is important that the record be permanent and on the person of the patient because (1) many years may have elapsed since the inoculation, which in any case, if performed in infancy, is beyond the patient's memory, (2) the patient may be unconscious, and (3) it is routine practice in many hospital receiving rooms to give antitetanic serum for all types of injury, even minor ones, in which the skin is penetrated. The only way of satisfying these requirements is by tattooing.

The desirable characteristics of such a tattoo are that it must be obvious when looked for and yet not conspicuous, and this immediately raises the question of position, for the site should be

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standardized, hidden, and yet easily available for inspection. The lateral aspect of the great toe, the inside of the lip, under cover of the ear over the mastoid, over the hip just below the iliac crest have all been suggested as possible sites, but the latter position seems, on the whole, the most suitable. Clearly, if the method is adopted the site and size of the mark would have to be established at a national or better an international level.

The author devised a tattooing instrument about the size of a fountain pen. It is in effect a spring gun which on being released drives a "bullet" through a paste of dye for a predetermined distance into the skin. The best dye for this purpose is ordinary commercial lamp black mixed to a paste with a little water and sterilized by heat. The bullet itself, the needle points of which alone penetrate the skin, can be sterilized by boiling or chemically by immersion in chloroxylenol in alcohol. A little of the paste is applied to the cleaned skin of the area, the bullet is inserted into the muzzle of the gun where it is held by a light spring, and the plunger is withdrawn to its full extent. The gun is applied firmly to the skin and the trigger is pressed. The tattooing is instantaneous and practically painless. The depth of penetration (usually 2 or 3 mm.) is controlled by adjustment of the screwed cap and depends on the thickness of the skin at the selected site and on the age of the patient.

Extra bullets (with other designs if necessary) can be accommodated in the hollow head of the plunger. Needle points prepared from stainless piano wire by grinding gave a better tattoo than the highly polished and smooth commercial article. The tattoo consists of a series of dots arranged in the form of a T, is easily identifiable but not conspicuous, and, like all tattoos, is permanent. It is probable that a tattoo performed in infancy will stretch with the growth of the child, but, although sufficient time has not elapsed to observe if this is so, it seems unlikely that it will be enough to render the mark unrecognizable.

Biochemical Diagnosis of Pheochromocytoma.—Vanilmandelic acid (VMA) has been identified as a major metabolite of both epinephrine and levarterenol and comparatively large amounts are excreted in the urine of patients with pheochromocytoma. Sandler and Ruthven developed a precise colorimetric technique for the assay of VMA (*Lancet* **2**:114, 1959). This depends on its conversion to vanillin which is assayed colorimetrically. The urine is passed through a cation-exchange resin and the absorbed VMA eluted with acetate buffer, extracted with ethyl acetate, and after evaporation of the latter converted into vanillin by heating with sulfuric acid in the presence of activated alumina as a catalyst. The vanillin is then assayed colorimetrically with indole in the presence of orthophosphoric acid. Patients with pheochromocytoma were found to have a urinary output of VMA from two to six times that of the normal subject. Except for bananas, which contain appreciable quantities of levarterenol, no dietary restrictions need be imposed in performing this test.

Radioactive Corpses.—A panel set up at the request of the Ministry of Health to advise on the disposal of radioactive corpses reported that the hazards associated with tracer amounts of radioactive materials used for diagnostic purposes are negligible in cadavers. Apart from temporary implants, therapy with radioisotopes is virtually confined to the use of P^{32}, Au^{198}, and I^{131}. The panel suggests that hospital physicists should be responsible for advising on radiation problems associated with the disposal of radioactive corpses and with postmortem procedures. When patients who have received therapeutic doses of radioisotopes are discharged from the hospital their doctors should be informed, and cremation, embalming, and autopsy should not be performed without reference to the hospital where treatment was given. No special precautions are necessary for morticians involved in the direct burial of such corpses, nor are they for the autopsy or embalming of corpses containing not more than 5 mc. of Au^{198}, 10 mc. of P^{32}, or 15 mc. of I^{131}. Corpses containing more than these amounts should not normally be embalmed.

These maximum figures do not apply to autopsies because of the greater frequency of these, and the continual exposure of the same staff to radiation from the corpses. If an autopsy is done the pathologist should consult with the hospital physicist, who will advise on the degree of radiation likely to be encountered. The panel advised that proper equipment, including rubber gloves, aspiration apparatus, and rubber tubing should be used. No special precautions are necessary for the cremation of corpses containing up to 30 mc. of I^{131} or Au^{198}, or 10 mc. of P^{32}. Temporary implants of isotopes should be dealt with in the same manner as radium containers and should be removed from corpses before removal from the hospital.

Bacillary Dysentery.—P. J. Taylor (*British Medical Journal*, July 4, 1959) treated a series of patients who had dysentery during an epidemic in Cyprus. Alternate patients were given either phthalylsulfathiazole or Streptotriad (a proprietary preparation containing in each tablet 65 mg. of streptomycin, 100 mg. of sulfathiazole, 100 mg. of sulfadiazine, and 65 mg. of sulfamerazine) for six days. The identity of the two kinds of tablet was concealed. In addition, kaolin and morphine mixture (B. P.) was given as required. The patients were seen daily and the duration of diarrhea and relapse rate were noted. After the six days of treatment

one rest day passed before the six consecutive daily stools were examined. The author found abdominal colic to be of little value for diagnostic purposes, since only some 55% of the patients had a temperature and this returned to normal in almost every case by the end of the second day. The author found that the cheap compound consisting of three absorbable sulfonamides and a small amount of streptomycin was superior to the single absorbable sulfonamide alone. The same issue contains a report by Falisevac and co-workers of Yugoslavia who corroborated Taylor's findings and also found the mixture superior to much larger doses of streptomycin alone.

How Much Medicine Should the Public Know?—Conflicting answers to this question were given at the British and Canadian Medical Associations' joint meeting at Edinburgh. Prof. D. M. Dunlop (Edinburgh) thought that the public should be educated in the broad principles of health rather than in medical knowledge. He agreed that the medical profession is not in agreement on how much the patient should be told about his disease. This largely depends on the level of his education. What the physician may tell an Oxford don is not the same as he would tell an untutored man. Dr. C. M. Fletcher (London) said that he was in favor of some education of the public and of patients, especially through the medium of television, because what was seen was more likely to be remembered than what was heard. He suggested that doctors could educate the public by describing the normal functioning of the body, paying special attention to the variations of function under the normal stress and strain of life, which might be mistaken by the anxious person as evidence of disease. Dr. Fletcher said that television programs dealing with disease had been criticized by doctors as pandering to the morbid interests of people, and were likely to interfere with the advice given by individual physicians, but he disagreed with this and thought that demonstrations of the achievements of modern medicine would dispel fear and increase confidence in the nervous and apprehensive patient.

Dr. R. Asher (London) said that it was impossible for intelligent persons to take no interest in their bodies. They are bound to form ideas about them and to seek information about health and disease. If medical information is not provided they may, like children, acquire wrong ideas. Some of these may be harmless and others may be harmful. On the other hand, too much information can be given, as in modern medical encyclopedias for the public, which do more harm than good. Dr. Asher thought it wrong for the public to learn from any source about new treatments, because some persons always thought that any new treatment was bound to be effective. He blamed in particular *Reader's Digest*, from which many persons obtained their information of what is new in medicine. Every doctor knows the patient who comes armed with this magazine demanding to have a particular form of treatment. It is better to give information that is cheering or helpful rather than that which does little good, but is frightening or depressing. If the public is aware of modern developments in medicine physicians themselves will see to it that they keep up with recent medical discoveries.

Raynaud's Disease.—At the same meeting, Dr. J. H. Peacock (Bristol) offered a new concept of Raynaud's disease. He has estimated epinephrine and levarterenol levels in the venous blood from the hand in patients with Raynaud's disease before and after sympathetic stimulation. The catechol amines are separated by chromatography and assayed biologically on the rat's blood pressure. They arise from peripheral sympathetic nerve endings and indicate sympathetic overactivity. In patients with thromboangiitis obliterans smoking cigarettes caused a sharp rise in the catechol amines in the blood in the inferior vena cava just above the level of the adrenal outflow.

In primary Raynaud's disease there is a low level of heat production and a low excretion of urinary estrogens and 17-ketosteroids, and a low plasma-bound iodine level. These changes indicate a new concept in treatment. Peacock gives reserpine to block the excessive production of catechol amines and to decrease their concentration in the arterial walls. Liothyronine and anabolic androgens, such as methandriol, are given to raise the metabolic rate and increase heat production. Vasodilator drugs were found to be of little help and difficult to control, and the late results of sympathectomy were unsatisfactory because of the return of vasomotor tone. Patients treated along these lines have been followed for three years, and the effectiveness of treatment proved by the effect on blood flow in their hands.

Electrogastrograms.—At the same meeting, Dr. H. S. Morton described how the electrogastrogram, originally designed for the detection of action currents in the stomach, could be used to diagnose lesions in the small intestine. The patient swallows a small silver chloride electrode, which is connected by thin wires to a modified Sanborn recorder. Its position is identified radiographically. Action currents caused by changes in potential reflect changes in the motility and amplitude of the contractions of the intestine. One of the uses of the electrogastrogram is to see whether vagotomy will be of benefit, because the activity of the intestine can by this means be measured objectively. The effect of new drugs on the motility of the stomach and intestine can be observed from a study of the electrogastro-

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gram. Obstructive tumors and hemorrhage also effect the record. Morton was careful to point out that changes in the electrogastrogram are not pathognomonic of any particular disease and that it is meant to supplement clinical and radiologic examinations, not to replace them.

Hydatid Disease in South Wales.—At the same meeting, Dr. L. R. West (Glamorgan) stated that although hydatid disease is considered rare in Britain there were 149 cases of human infection in South Wales in 1957-1958. The case fatality rate was 9%. The liver was involved in 44% and the lungs in 43%. Dogs are probably the principal source of infection. A random survey of 50 town and country dogs in South Wales showed that 4 were infected. Bovine and ovine infection, which may be another source, has not decreased over the last 25 years. Thus, 0.9% of 23,632 carcasses examined at a Cardiff abattoir in a three-month period harbored hydatid cysts. This was twice the figure found in an examination of carcasses 25 years ago.

Monday Morning Illness.—At the same meeting, the results of an investigation into the epidemiology of Monday morning illness, another name for byssinosis, the occupational disease that affects those exposed to cotton dust, were described by Dr. R. Schilling (London). The disease is characterized by a tight feeling across the chest with dyspnea on starting to work in the cotton factory on Monday mornings, and relief of symptoms when ceasing work. Those in the carding rooms, who are exposed to cotton dust more than other workers in the industry, are affected the most. The incidence of disease varies directly with the amount of cotton dust in the air and with the amount of protein in the dust. The maximum breathing capacity, calculated by multiplying the volume of air breathed out in 0.75 seconds by 40 subjects, was found to fall sharply during the working day in those suffering from byssinosis. This reduction did not occur when they were working away from cotton dust, nor did it happen in workers in other dusty occupations, such as coal mining.

The effect on respiration is not an allergic response because normal subjects, without previous exposure, were affected if they remained in the carding room exposed to the dust for three hours. Workers with a history of prolonged exposure suffered from lung damage. No correlation was found between the bacterial and fungal counts of the air of the rooms that caused respiratory symptoms. Inhalation of dust containing bacteria and fungi by volunteers had no immediate effect on respiration, but cotton leaf dust when inhaled produced the symptoms typical of byssinosis. The substance responsible is water soluble, heat resistant, and probably polypeptide in nature, but has not been isolated. An extract of cotton leaf dust was found to produce contraction of the guinea pig tracheal muscles.

Psychoses in Infancy and Childhood.—At the same meeting, Dr. W. A. Hawke (Toronto) reported that a detailed history, a careful examination of the child, and an appraisal of the parents through interviews and psychological studies were made in 150 cases of childhood psychoses. The parents were generally highly intellectual, with an average IQ of 120 in one group. Many of them had intellectual, artistic, and musical interests. The psychological analysis of the parents in one group revealed that less than 10% were normal, the remainder being moderately neurotic or overtly schizophrenic. In another group of parents 20% were classified as normal, 60% as severely neurotic or schizoid, and 20% as ambulatory schizophrenics, some of whom had been hospitalized. In both groups of parents examined a number of positive family histories of schizophrenia were obtained. It is concluded that children with psychoses are born into families in which there is a significant tendency toward schizophrenic disturbances.

In a number of these families the parents were not successful in life in spite of high intelligence and education. They tended to occupy positions below their potential capacity and their incomes were less than would be anticipated from their training. Many of the parents could not plan or organize a suitable routine for their children. In a number of cases there was a significant disturbance in the early relationship with emotional deprivation of the child. It was concluded that two factors, constitutional and environmental, are present in most cases of psychoses in childhood and tend to reinforce one another. In general, the greater the constitutional factor the poorer the prognosis, since the basic defect is resistant to therapy. The greater the environmental factor the better the prognosis because this factor may be improved by therapy. In some cases where the parents are frankly schizoid or schizophrenic little can be done unless the child is separated from the family.

Spinal Acrylic Inlays.—Immobilization of acutely painful or unstable spinal joints by bone grafts is a logical method of relieving pain, but bone grafting involves lengthy operations and prolonged hospitalization. Rib inlay grafts give satisfactory support for a time but some soften. Knight reported on the use of paraspinal acrylic inlays instead of bone (*Lancet* **2**:147, 1959). The use of acrylic for skull reconstruction, inserted when it is of doughy consistency, and hardening in the tissues within 24 hours, has already proved successful, and excites no significant tissue reaction. The degree of hardness resulting compares favorably with that of pressure-heated material.

The powdered acrylic polymer, Kallodent 222, is sterilized by autoclaving in bottles or a metal container. The liquid acrylic monomer is sterilized by filtration. Twenty minutes before the inlay is required one part of monomer is poured evenly over 3.5 parts of polymer. After about 20 minutes the consistency is tested with a sterile spatula. If still tacky it is allowed to harden. Inlays of 1.7 cm. are used in the lumbar spine and half this thickness is used in the cervical spine. An inlay of appropriate size for the cavity exposed is cut from the material and when dry and rubbery it is inserted into the wound. After the insertion of the plastic between the lamina and paravertebral muscles the spine is supported in the optimum position for 24 hours, which allows the inlay to mold itself over the bones. The secret is in having the inlay of the right consistency. If it is too wet a serous effusion may occur.

Knight has used these paravertebral inlays for the relief of spondylosis, osteoarthritis, chronically painful fracture-dislocations, and the stabilization of atlantoaxial subluxations. The effect is produced by reduction in movement at the level of the painful joint. After operation an extremely good range of spinal movement is provided by the joints above and below the site of immobilization. The patient is operated on in a sitting position. Through a midline incision the paravertebral muscles are dissected to expose the backs of the laminae on one side only. After complete hemostasis the inlay is used to completely fill the space over the laminae before the paravertebral muscles are resutured.

Psychosis and Addiction to Phenmetrazine.—Phenmetrazine is a sympathomimetic drug, with an action similar to that of amphetamine, used for the treatment of obesity. Evans treated a series of 16 patients who had become ill from taking the drug in large doses, 12 of whom were addicted to it (*Lancet* 2:152, 1959). Nine had symptoms that were indistinguishable from those of an amphetamine psychosis. They had delusions of a paranoid, nihilistic, and depressive type, hallucinations, and disturbances of affect. Two patients were disoriented. All recovered after hospitalization for a week, but four patients had relapses after discharge and started taking increasing quantities of the drug. The history of an excessive intake of phenmetrazine, a frank psychosis, and its resolution on stopping the drug justifies the term phenmetrazine psychosis.

A second group of five patients had a delayed recovery. All had taken 10 to 20 tablets of phenmetrazine for weeks or months. The symptoms of two of the patients resembled those described. Two had a definite schizophrenic thought disorder with vagueness and bizarre associations. If consumption of the drug is concealed the psychosis due to it cannot be distinguished from other psychoses. Most of the patients were women who had taken phenmetrazine to help them reduce. Others had taken it to restore energy. Thirteen had taken drugs, alcohol, or amphetamine derivatives previously. Their work record was unstable, as all had changed jobs frequently. Three patients said that in certain coffee bars and clubs in London phenmetrazine is used frequently as an energizer. Phenmetrazine is definitely a drug of addiction and it should be obtainable only on a doctor's prescription, which cannot be refilled.

Olympic Games.—Doctors and scientists will accompany the British athletes to the Olympic games in Rome next year. They will help to reduce the effects of exposure to unaccustomed sunlight, heat, and humidity, and help the athletes to adapt themselves to different foods. A drop of only 2% in efficiency can reduce an athlete from the first to the sixth place in the competition. Athletes are prone to gastric and digestive upsets which the doctors attending the team hope to prevent. Suggestions to be considered are that the British team should train for a period in heavy track suits to acclimatize themselves to exercise under hot climatic conditions, and to receive sun-ray treatment before leaving Britain. The Medical Research Council and the British Association of Sport and Medicine will advise on adaptation to new climatic conditions.

Labor Party's Plan for Health Service.—Political parties are always active when a general election is imminent. As another government is likely to be formed this fall the Labor party has produced a new health program which they propose to implement if returned to power. Although there is public concern over the annual cost of the National Health Service (nearly 2,000 million dollars) the Labor party suggests spending another 300 million dollars on it. The details were given at a press conference recently and in a party publication. It is proposed to spend 150 million dollars a year on new hospitals. Capital spending on the hospitals is now running at about 75 million dollars annually, which is about one-third of what the British Medical Association recommended. Labor's argument is that in an expanding economy the proportion of the national income spent on health should rise.

One proposal in the Labor program is that the 21,000 government-paid general practitioners should have fewer patients on their lists than at present. This would be achieved without reducing their income. Labor admits that general practice is the Cinderella of the service and that the general practitioner works hard under intolerable conditions, with his wife as an unpaid worker in the service. About 25% of the population are on the lists of doctors with more than 3,000 patients. Labor's goal is 2,500, although it does not propose how this should be done without more doctors. An appointment system for visits to the doctor's office is proposed be-

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cause the public wastes millions of hours every year waiting to see general practitioners. Group practice by general practitioners will be encouraged by loans to acquire new offices. Many doctors' offices are still dirty, dingy, and poorly equipped according to the report. All charges for medicaments are to be removed and employers are to pay more toward the cost of their employees' health.

Teaching hospitals enjoy comparative independence at the moment, with their own boards of governors. This will be lost if the Labor proposals are implemented. These hospitals will be integrated with the regional hospital boards. The new order wishes to encourage research, particularly in the nonteaching hospitals, and to extend the industrial health service, which at present is paid for by private industry. Medical education, particularly in London's 12 medical schools, is to be the subject of government inquiry. The Labor party believes that medical education in London is dominated by the views of specialists on Harley Street, and is thus isolated and insulated from the realities of medical work as most doctors have to practice it. The party aims to give further responsibility to regional boards and management committees, and to reduce paper work, meetings, and bureaucracy in the administration of the hospitals.

The present mental health services come under criticism. They have been deprived of money for years the party states. A major building program of psychiatric units in general hospitals is proposed, with extension of the social services for the community care of the mentally sick. Increased facilities for their home care is suggested. A free mobile chiropody service for older persons and a mobile physiotherapy service are also recommended. To remedy the shortage of dentists Labor plans to encourage the recruitment of dental students. In 10 years the nation's drug bill has risen from 98 million dollars a year to 176 million dollars. Labor hopes to reduce this by supplying doctors with information on the nature and price of drugs prescribable under the health service. Doctors would be informed monthly of the cost of their prescriptions to the state, and vigorous attempts would be taken to reduce the price of drugs. It is pointed out that more money is spent on the drugs prescribed than on the doctors who prescribe them. The party considers that private beds in state-owned hospitals are an anomaly, and hopes that they will soon disappear.

More bureaucratic control is promised to doctors in partnership. Permanent assistantships and assistantships without a view to partnership will be made unlawful. All partnership agreements will have to conform to standards laid down nationally and be approved by local executive councils before signing. The Medical Research Council is criticized. Of 840 million dollars a year spent on research in the country, only 22.5 million dollars is spent on medical research. The Labor party considers that the Medical Research Council must revise its approach and create many more research posts so that practical problems may be tackled by large teams. Many of these proposals and criticisms come from a party that forced a hastily conceived National Health Service on an unwilling medical profession, and is itself responsible for some of the shortcomings of the service. The Labor party's criticism of the Medical Research Council is irresponsible. This body does excellent work on its meager budget.

Strontium-90.—The Radiological Laboratory of the Agricultural Research Council has published a report entitled "Strontium-90 in Human Diet in the United Kingdom" (Her Majesty's Stationery Office, 1959). It concludes that the average amount of radioactive strontium (Sr^{90}) in the food and water of persons living in Britain is about 17% of that which would call for action. Some diets include a higher intake than others, but no foods have a content at present considered dangerous. The level recommended by the Medical Research Council above which action should be taken is 40 μc per gram of ingested calcium. At present the average British diet contains 6 μc per gram of calcium.

The danger of Sr^{90} is that it is metabolized in the same way as calcium and deposited in the bones. Although few persons consume diets containing more than 10 μc of Sr^{90} per gram of calcium, diets in certain limited areas may contain as much as 23 μc of Sr^{90}. In these areas the environment would lead to the rapid transfer of Sr^{90} to the diet. Some foods such as whole wheat bread and milk contain a high proportion. Whole wheat flour not only contains more Sr^{90} than white flour, but it has no added calcium carbonate as has the latter. Calcium added to the diet decreases the amount of strontium absorbed as it is taken up preferentially by the skeleton. Sr^{90} is in the fall-out of atomic explosions, although only that which has fallen out in the preceding one or two months is likely to be found in food in any quantity. There is a delay of this period from the time of fall-out to the appearance of Sr^{90} in milk. It is very persistent, the half-life being 30 years.

The delay between the fall-out and the entry of Sr^{90} into the food shows that the amount in the diet is not the result of the accumulation of successive quantities in the atomic fall-outs since 1945, when the first nuclear weapon fell. When it is washed well into the soil it becomes less and less accessible to plants and animals. An increase of Sr^{90} in food and water during the current year is likely because many bombs were recently exploded and it is likely to persist for a time. The report points out that the amount of Sr^{90} absorbed from the food could be decreased by increasing the calcium intake, which could be done by adding it to flour.

CORRESPONDENCE

MICROSCOPIC HEMATURIA

To the Editor:—In the Aug. 15, 1959, issue of THE JOURNAL, page 2014, in the Correspondence section, is a statement by Dr. Bruce H. Stewart concerning the number of erythrocytes found in urine and the interpretation of this number. He objects to a widely circulated brochure stating that in centrifuged urinary sediments the normal number of erythrocytes per high-power field varies from 4 to 10. Dr. Stewart concludes "that more than one red blood cell per rare high-power field in a routine centrifuged urinary sediment must be considered abnormal."

It is never possible to give quantitative results from a procedure which is not carried out in a manner designed to yield such results. In neither one of these references is any standard procedure set up for determining the number of cells per high-power field. Actually, even the high-power field is not defined. Some persons examine urine with a 5X ocular, while others use a 10X ocular, and some consider an 8-mm. objective as being of high power while others consider a 4-mm. or even a 3-mm. ocular to be of high power.

The report by Greene at the Mayo Clinic cited in the letter by Dr. Stewart was based on a standard procedure which has been used in the Section of Clinical Pathology for many years. Although the laboratory work itself is rigidly supervised, there is no supervision of the actual collection of the specimens, and these results may be based on anything from a single-passed specimen to a 24-hour collection of urine. This in itself may make a great difference in the number of cells found in a high-power field.

When the urine is delivered to the laboratory, it is shaken and 14 ml. is poured into a 15-ml. conical centrifuge tube. The tubes are centrifuged in a no. 2 International centrifuge with a 16-place, 15-ml. head, at 1,800 rpm, for eight minutes, the time being measured from the moment when the centrifuge has reached its maximal speed. The supernatant is poured off, leaving about 0.5 ml., which is shaken, and then one drop is poured from the centrifuge tube onto a glass slide and a 22-by-22-mm. cover slip is applied. This gives a fairly "thick" preparation. Six high-power fields are counted with use of a 4-ml. objective and a 10X ocular. The numbers of cells in the six fields are averaged to give the count.

It can be seen that any one of a number of factors, if varied, can produce a marked difference in the results. For example, if the preparation is one-half the thickness described above, the number of erythrocytes per field will be reduced about 50%. Variations in the centrifugal force applied to the specimen also will give great variability in the results. It is possible, if the standard used at the University of Michigan Medical School is based on a smaller amount of urine which is centrifuged for a shorter period and with less centrifugal force, and if the high-power field is one obtained with a 5X ocular, for one red blood cell per high-power field to constitute a relatively large amount of blood as compared with the figure which forms the basis for the report by Greene or the figure given in the brochure referred to. Attempts to read laboratory results too finely and too dogmatically have led to many errors, and one should be cautious in taking over the laboratory reports from one laboratory and applying them to another. One swallow still does not make a summer, and one erythrocyte does not make a diagnostician out of a sophomore.

T. B. MAGATH, M.D.
Section of Clinical Pathology
Mayo Clinic
Rochester, Minn.

DIHYDROSTREPTOMYCIN DEAFNESS

To the Editor:—In THE JOURNAL, Aug. 1, page 1657, is an important article entitled "Dihydrostreptomycin Deafness," in which the authors have set down a report concerning 32 cases of deafness occurring after administration of dihydrostreptomycin. This fairly transcontinental study from the four points of the compass in the United States shows the extent to which antibiotics are administered. Penicillin, the first of these, was found to be of tremendous value, but since it did not prove effective in every instance, combinations of antibiotics were used with better results. Then streptomycin, discovered by Waksman, was heralded and it seemed that many sufferers were relieved of tuberculosis, although some patients had impaired hearing or visual disturbances after use of the drug.

Then Glorig, in 1951, reported on the effect of dihydrostreptomycin hydrochloride and sulfate on the auditory mechanism (*Ann. Otol. Rhin. & Laryng.* 60:327-335 [June] 1951), an initial contribution which had to do with tuberculous patients who had received this drug in doses of 2 to 7 Gm. weekly. Irreversible deafness was noted three weeks to five months later. Then came combinations of other antibiotics with such names as Combiotic, Dicrysticin, Distrycillin, Strocillin, and Durycin.

The previously mentioned 32 cases of deafness from dihydrostreptomycin occurred after administration of the drug to patients with cystitis, influenza, tuberculosis, pleural effusion, asthma, nephritis, panhysterectomy, furuncles, respiratory infections,

pneumonia, appendectomy, mononucleosis, sinusitis, and encephalitis. The latent effects, especially deafness, came on weeks or months after administration of dihydrostreptomycin in combination with penicillin or other antibiotics. A small dose of dihydrostreptomycin may be sufficient to produce deafness. Both ears are affected equally, and the loss runs from 20 to 70 decibels.

Fifty years ago I began work in otology in the old Politzer clinic in Vienna. The Wassermann test had just come out, and it was claimed that arsphenamine would "cure syphilis at one shot." Many patients so treated became deaf. Clinicians did not know then that it was the impurities in the arsenic which were responsible for deafness. History now seems to have repeated itself.

Irving Wilson Voorhees, M.D.
35-26 79th St.
Jackson Heights 72, N. Y.

COMPLICATIONS FROM CHLORPROMAZINE

To the Editor:—The account by Floch and Leibowitz in The Journal, Aug. 22, 1959, page 2060, entitled "Hemorrhage from Multiple Sites Associated with Chlorpromazine-Induced Jaundice" adds yet another to the long list of complications resulting from the use of chlorpromazine. The comment concerning the appearance of hyperglycemia in the patient under discussion indicates that this was believed to be an independent finding related to a coincidental occurrence of diabetes mellitus. It may be worthwhile to point out that the hyperglycemia in question may not be an independent and accidental occurrence of diabetes mellitus but may, in fact, be due to the chlorpromazine.

Hiles, in The Journal, Dec. 29, 1956, page 1651, described a number of patients who developed hyperglycemia and glycosuria while receiving chlorpromazine. In some of these the effects disappeared after the cessation of the drug therapy. Charatin and Bartlett published a report, abstracted in The Journal, Sept. 10, 1955, page 145, on an investigation into the hyperglycemic effect of chlorpromazine in man. It would be of interest to know whether the patient described by Floch and Leibowitz is still considered diabetic or whether the hyperglycemia was transient.

George X. Trimble, M.D.
Director of Medical Education
Seaside Memorial Hospital
Long Beach, Calif.

The above comment was referred to the authors of the article cited, and the following reply has been submitted.

To the Editor:—The comment by Dr. Trimble is of interest. The observation of fasting hyperglycemia early in the course of our patient with chlorpromazine-induced jaundice led to the performance of a glucose tolerance test on the 10th day of her illness. This was typical of diabetes mellitus. It was duplicated when the test was repeated on the 42nd day after the onset of illness when all evidences of liver dysfunction had disappeared and she had long abstained from the drug. Available follow-up information failed to clarify whether this hyperglycemia and abnormal glucose tolerance were transient or persistent. No similar data have been obtained thus far since her discharge. At no time did random urine samples reveal glycosuria, either during the illness or in the follow-up period. There was no diabetic history prior to the illness and no family history of diabetes. In preparing our paper we were at first struck by the apparently frequent occurrence of diabetes mellitus in reported cases of chlorpromazine-induced hepatitis as well as in patients we had previously observed, but when these were actually counted we could find no greater incidence than chance would explain. It is for that reason that we concluded that the diabetes mellitus was an independent coincidental finding.

Sidney Leibowitz, M.D.
15 W. 54th St.
New York 24.

HYPERURICEMIA

To the Editor:—I have read with interest the paper on the relationship of hyperuricemia to hypercholesteremia and acute myocardial infarction by Kohn and Prozan (*J. A. M. A.* **170**:1909-1912 [Aug. 15] 1959). The authors implied that the hyperuricemia seen in their patients was a hereditary defect and gave no information as to other possible causes of hyperuricemia in this group. Hyperuricemia may be due to several causes other than heredity. The most common is chronic renal insufficiency. It would be of great interest to learn the frequency of blood urea nitrogen elevation among the 50 patients reported on in this paper. Also information should be given as to the possible presence of blood dyscrasias that are associated with hyperuricemia (Talbott: *Medicine* **38**:173 [May] 1959; Gutman: *Ann. Int. Med.* **39**:1062 [Nov.] 1953). Finally, in a group of patients with acute myocardial infarction, it is possible that some were receiving chlorothiazide for either congestive heart failure or hypertension. Laragh and others (*J. A. M. A.* **166**:145-152 [Jan. 11] 1958) have shown that this drug causes uric acid retention. Even if none of these factors is operative in the patients reported on by Kohn and Prozan, such negative information is important and should have been included in the paper.

Stanley L. Wallace, M.D.
1122 Ocean Ave.
Brooklyn, N. Y.

THE LEISURE CORNER

COLLECTING OF MUSICAL BOWS

When a Frenchman named Françoise Tourte perfected the art of bowmaking in the late 1700's, he introduced into the musical world a device that has become the magic wand of many musicians. Everyone knows that the violin, the best known and mostly widely used of all string instruments, requires a bow, which is usually a curved stick about 27 in. long, containing about 150 horsehair threads stretched from the tip to an adjustable frog. The musical tones of the violin are made by pulling the bow back and forth over the strings. It was Tourte who lengthened the bow, reversed its curve, and made it lighter and more willowy than the earlier types of bows had been. The first bows were curved like the weapon of the same name. The bow probably originated in the Orient, and was introduced to Europe during the Crusades.

The earliest use of bows on stringed instruments is shrouded in mystery. Whether a stringed instrument was first played by plucking or bowing is still undetermined, although it is generally maintained that plucking had precedence. Ancient Persians always plucked their instruments, while some of the Asiatic peoples such as the mountain and island dwellers of India "bowed" their instruments. It was not until the Persians eventually came into contact with other races that they became acquainted with the use of the bow. In like manner, the inhabitants of the shores of the Mediterranean Sea learned to pluck their instruments, while the Gothic peoples, chiefly Germanic in origin, identified their urge for musical expression with the use of the bow. The earliest bow, which dates back to about 1000 A. D., resembles a branch; it appears as a pliable reed held in a bent position by threads, strings or horsehair, tied at each end.

It was not until the 17th century, when the violin evolved into its present form, that more accurate and definite information about the bow was introduced. Henry Saint-George, author of "The Bow," has this interesting comment to make: "I wonder whether violinists often realize when they take up a bow how many remote parts of the earth have contributed to this little magic wand! Wood from the West, ivory from the East, mother of pearl from the sea, gold or silver from eastern, western, or it may be Antipodean mines; and when we add thereto the hair from the horse's tail, and we levy a tax upon the three kingdoms, vegetable, animal and mineral, to minister to our enjoyment." As for construction of the bow, the greatest concentration of precious wood employed in making fine bows is found in the forests of Pernambuco, one of the coastal regions of Brazil. In addition to the utilization of Pernambuco wood and brazilwood, the woods probably most commonly used in bow-making are derived from beech and snakewood. The markings one sometimes sees on bows, wherein the grain resembles the splotches or rings of a snake, identify the source of material. Ebony is still another type of wood employed in the construction of a bow, but this is second in importance to Pernambuco wood, which is often selected because of its hardness and its ability to resist wear.

Many doctors have become collectors of bows used in conjunction with the violin, viola, violoncello, and double bass. The hobby frequently consists in selecting bows that were built many generations ago right down to those constructed at the present time. As in the case of the hobby of collecting valuable paintings, a bow made by a good maker, in excellent condition, with perfect mountings, and possessing a fine playing quality becomes a valuable possession. Prices commanded by bows depend on construction, craftsmanship, and design. Collectors are known to look for fine bows all over the world. They seek a graceful tapering of the stick, the proper length, elasticity and flexibility, the precise balance of size and weight of head and frog, the proper method of fastening the hair with ferrule and slide at the frog so as to hold it in a flat ribbon, the exact fitting of frog to stick. Each one of these details in a bow is conceived and executed with meticulous care, exactness, and artistry.

Doctors do not necessarily have to be accomplished musicians themselves in order to appreciate the considerable artistry that goes into the making of a superb bow. When purchasing a bow as a collector-hobbyist or a musician or both, it is well to investigate the condition of the bow, with attention paid to certain details; for example, the presence or absence of cracks in the head, tip, shaft, and frog. Indeed, the stick should be straight and devoid of bad knots or other imperfections, while the frog should sit closely and accurately to the stick. Since an increasing number of people have evinced growing interest in bows in recent years, the value of a bow as a work of artistic construction and as an important musical-playing adjunct has become more widely recognized. More expert concern, as a result, has developed among dealers, musicians, connoisseurs, and collectors.

The cost of a fine bow, made by an "old master," has like all other items in our economy, mounted. At the beginning of the 20th century seven excellent bows by Françoise Tourte commanded a catalogue price ranging from $125 to $300. Today, a good Tourte bow is rarely offered for sale, and even when it is obtainable the price is at a premium. Similar high prices hold true for bows made by such fine makers as Vuillaume, Dodd, Lupot, Eury, and Voirin. Fine examples of their work are scarce, yet at the same time they are more appreciated, since appreciation of fine construction has grown. The increased scarcity of exceedingly fine bows is due to the fact that some of them have been broken over the years, while others have been damaged beyond repair.

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V. 1

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Postviral Myopericarditis Associated with the Influenza Virus: Report of 8 Cases. C. W. Adams. Am. J. Cardiol. 4:56-67 (July) 1959 [New York].

During the influenza epidemic of 1957-1958 the author observed 8 patients with acute "nonspecific" pericarditis, who had a fourfold rise of serum antibodies against the influenzal virus. The latent period of one or more weeks between the acute influenzal attack and the pericarditis suggests that an allergic or a hypersensitivity mechanism is involved. The laboratory evidence demonstrated in 5 cases the type B (Great Lakes) influenza virus; in 2 cases both type A (Japanese) and type B viruses; and in 1 case the type A virus. Acute "nonspecific" pericarditis is not necessarily "benign," as it is frequently associated with myocarditis, pericardial effusion, pleurisy, pleural effusion, and pneumonia. These features may be more appropriately designated as acute myopericarditis.

Seven of the 8 patients presented were males. One patient was a woman in whom the pericarditis occurred at the time of delivery and during the postpartum period. For many years, instances of "postpartal heart disease" have been reported without a previous history or clinical findings of heart disease. In fatal cases, the myocardium has shown moderate infiltration of lymphocytes and macrophages. It has been pointed out that "postpartal heart disease" is probably not due to a specific entity or even necessarily related to pregnancy or the puerperium, but may be related to one of a number of different etiological agents. All patients with "postpartal heart disease," atypical myocardial infarction, or acute "nonspecific" pericarditis should be carefully evaluated for the recent presence of viral diseases as a possible cause of the cardiac difficulty. The hemagglutination inhibition influenzal antibody titer determinations are recommended in all cases of acute "nonspecific" pericarditis in an effort to further classify these cases. The history and the clinical and laboratory findings in these 8 cases of "nonspecific" pericarditis suggest that this cardiac disorder is, in fact, a myopericarditis, and the term "postviral myopericarditis" is suggested in preference to acute benign "nonspecific" or "idiopathic" pericarditis.

Effects of Lanatoside C on Cardiovascular Hemodynamics: Acute Digitalizing Doses in Subjects with Normal Hearts and with Heart Disease Without Failure. D. T. Dresdale, Y. Z. Yuceoglu, R. J. Michtom and others. Am. J. Cardiol. 4:88-99 (July) 1959 [New York].

Patients with heart disease but not in failure are frequently considered for prophylactic digitalization prior to major surgery or other types of unusual stress. If no deleterious effects on the cardiovascular hemodynamics are demonstrated, such therapy might well be justified. This report presents the early effects of lanatoside C on the cardiovascular hemodynamics in 11 patients studied by the technique of right heart catheterization. Seven of the 11 patients had normal hearts, and the other 4 patients had heart disease without clinical or hemodynamic evidence of heart failure. Lanatoside C in full therapeutic doses caused no significant changes in cardiac output, heart rate, systemic venous, right ventricular systolic, and pulmonary artery pressures. The systemic arterial pressures and resistances similarly were not appreciably affected. In 2 of 8 cases, there was a slight fall in the right ventricular end-diastolic pressure, and in 5 of 6 cases there was a slight fall in right auricular pressure. Interpretations of the presented data were made on the basis of control studies, but it is pointed out that there are difficulties in interpreting the changes in cardiac output in this type of study.

The problem of whether prophylactic digitalization is useful in patients with heart disease but not in heart failure was not solved by this study. Nevertheless, it is felt that these patients can be digitalized without fear of decreasing cardiac output or producing unfavorable changes in blood pressure.

Heart Disease and Influenza. G. Bourne and J. Wedgwood. Lancet 1:1226-1228 (June 13) 1959 [London].

The authors present observations on 14 patients, observed during the 1957 epidemic of influenza, in whom influenza appears to have been the cause of cardiac disability. Auricular fibrillation was pre-

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The place of publication of the periodical appears in brackets preceding each abstract.

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cipitated in 8 patients, and auricular flutter in 1. Symptoms of coronary artery disease were initiated in 2 patients. Two other patients with angina of effort due to coronary artery disease, who were being studied by serial exercise tests, became worse after an attack of influenza. Their angina became more severe, and objective evidence of deterioration was obtainable from exercise tests. Finally, in one patient influenza seems to have caused an inversion of the T wave in the left ventricular leads, but this reverted to normal during convalescence.

After describing the case histories of the 14 patients, the authors point out that in 4 of the 8 patients with auricular fibrillation there was no evidence of any other cardiac abnormality; in the other 4 the electrocardiogram revealed signs of an underlying myocardial defect. In the patient with auricular flutter the abnormal rhythm seemed to be due entirely to the acute influenzal infection. Influenza appeared to initiate angina of effort in 2 of the 4 patients with coronary symptoms, and to accentuate the ischemic state in 2. In these latter 2 patients influenza also increased the electrocardiographic abnormality. In the last case the long history of premature beats, and later of paroxysmal tachycardia, pointed to some chronic but slight cardiac abnormality. Thus, in 6 of the 14 patients influenza would seem to have caused definite cardiac complications, and in the other 8 to have brought them to the surface. The ages of the patients, ranging from 47 to 70 years, with an average of 57, suggest that in all of them the heart may not have been perfectly normal. Influenza appears to have a definite, although transitory, toxic effect upon the myocardium.

The Incidence of Arteriosclerotic Heart Disease Among Cirrhotics. J. B. Berrios and R. C. Rodriguez. Bol. Asoc. méd. Puerto Rico **51**:205-211 (June) 1959 (In English) [Santurce].

The material for this study was selected from 3 sources: records of 1,276 autopsies performed at the Bayamón District Hospital in Santurce, Puerto Rico, during the period 1955-1958, and records of 2 groups of patients treated at the same hospital. Five groups of subjects were studied. Group 1 comprised 66 cases in which the cause of death had been arteriosclerotic heart disease. The average age of the patients at death was 66.5 years. There was no record of Laennec's disease among these cases. Group 2 comprised 9 cases in which the cause of death had been Laennec's cirrhosis. The average age of the patients at death was 41.5 years. There was no record of arteriosclerotic heart disease among these cases. Group 3 comprised 100 records of autopsies taken at random. There were 20 cases in which arteriosclerotic heart disease had been the cause of death, and among them only one patient had also had hepatic cirrhosis. Group 4 was composed of 84 patients with the clinical diagnosis of cirrhosis of the liver. The mean age in this group was 52.5 years. Nine patients (10.7%) in this group had also arteriosclerotic heart disease. Group 5 was composed of 50 patients taken at random from among those who had been given a diagnosis of arteriosclerotic heart disease at the Bayamón District Hospital. The average age in this group was 67.8 years. None of these patients had concomitant hepatic disease.

Comparing the respective incidences of the two diseases in the groups under study, it was found that the incidence of arteriosclerotic heart disease in the groups with a diagnosis of hepatic cirrhosis (10.7%) was much lower than the percentage of incidence in the general Puerto Rican population (25%). This finding also tends to show that cirrhosis of the liver may protect the patient against atherosclerosis. This "protection" is attributed to the changes in lipid metabolism which take place because of diffuse parenchymal hepatic disease, with consequent lowering of plasma cholesterol and phospholipids. If the findings in this study are corroborated, they may also explain the low incidence of atherosclerosis among the Oriental and Bantu populations who have a high incidence of liver disease.

Cytological Diagnosis of Sputum with Feulgen's Test in Cancer of the Lung: Note II. G. Angrisani, G. Curzio and S. Musella. Acta med. ital. **13**:151-158 (June) 1958 (In Italian) [Rome].

Early morning sputum derived from spontaneous cough of 50 patients with pulmonary disease was subjected to Feulgen's test. Thirty-four patients had or were suspected of having pulmonary carcinoma, 12 had pulmonary abscess, and 4 had bronchiectasis. Feulgen's test was positive in 31 of the 34 patients with pulmonary carcinoma. The authors believe that in the other 3 patients the anatomic location of the tumor was responsible for the negative results. A round-shaped neoplastic mass at the base of the superior right lobe was seen on roentgenographic examination in 2 of these patients, but cytological examination, which was repeated 5 times, always gave negative results. Anatomic examination of the lung after surgical removal showed an intraparenchymatous tumor formation, small in size, with no lesion of the large and medium bronchi. Only a small bronchial branch, closely connected with the peripheral area of the neoplastic tissue, presented light ulceration of the mucosa and infiltration of the other layers. No other significant histological involvement of any bronchial lumen was present in these 2 patients. The third patient had a bronchial adenocarcinoma. Histologically the adenocarcino-

matous proliferation did not invade the bronchial surface; the bronchial mucosa covered the tumor that protruded into the bronchial lumen. In this patient, too, the authors believe that the negative results of the cytological test may have been due to the absence of neoplastic exfoliative cells in the bronchial lumen.

Carcinoma was discovered through Feulgen's test in 4 of the other patients who on roentgenologic examination had presented a pulmonary suppuration. The authors point out that a good feature of Feulgen's test is that it eliminates the most serious errors due to false positivity. Negative results of the test in patients with carcinoma of the lung may be connected with the process of exfoliation of the tumor, or they may be the result of a transient occlusion of the air passages, clogged with mucus, which is likely to occur in cases of regional inflammation.

Pneumonia in the Aged. J. C. Gerrits. Nederl. tijdschr. geneesk. 103:1109-1112 (May 23) 1959 (In Dutch) [Amsterdam].

The clinical course of pneumonia has become milder. Particularly in elderly persons it frequently takes a milder, atypical course, but it nevertheless may terminate in death. Staphylococcic pneumonia, so often observed in the course of influenza epidemics, takes a definitely atypical course. Among 69 pneumonia patients in whom the author made bacteriological studies, 39 had pneumococcic pneumonia, 15 had a mixed bacteriological flora, 4 had pneumonia due to Staphylococcus aureus, and the remaining 11 patients had mostly Hemophilus influenzae and Streptococcus organisms.

The author is concerned with studies on the duration of pneumonia, which he investigated in 313 patients who were observed from July, 1955, to July, 1957, at 2 Amsterdam hospitals (170 receiving hospital treatment, and 143 being observed at the polyclinic). Since observations on younger patients had demonstrated that resolution of the pneumonic process is usually complete within one month, the author classified the patients not only with regard to age but also according to the time elapsed between onset and recovery. Fifty-two of the patients died, all but 5 of the deaths involving persons over 50 years of age. Disorders of circulation and respiration were frequent in the patients who died, but the nature of the causative organism apparently was of no importance. In 154 of the 261 surviving patients, the course was prolonged beyond one month. Retardation of recovery was especially frequent in patients over 50. In this age group recovery required more than a month in 75% and more than 2 months in 32% of the patients, whereas in patients under 20 the comparative percentages were 32 and 12%. Delayed recovery was chiefly due to respiratory disorders (bronchitis, asthma, or emphysema) or to circulatory disorders (myocardial degeneration, arteriosclerosis, and mitral stenosis).

The Treatment of Allergy to Ragweed Pollen by Means of a Single Annual Injection of Emulsified Pollen Extract: VI. Discussion of Results, Relationships and Some Miscellaneous Factors. E. A. Brown, Ann. Allergy 17:358-379 (May-June) 1959 [St. Paul].

During the year 1958 Brown treated 1,029 patients who had disorders caused by allergy to ragweed pollen. Of these, 344 received either from him, or under his supervision, standard pollen extract prepared in isotonic sodium chloride solution and given according to the multiple visit type of injection program. (Observations on the 344 patients will be presented in a separate report.) The other 685 patients were treated with a single preseason injection of an emulsified pollen extract, the emulsifying agent consisting of 1 ml. of Falba and 1.5 ml. of mineral oil (liquid petrolatum) for 0.5 ml. of pollen extract. Falba is an emulsion stabilizer which (according to Loveless) contains beeswax, paraffin oils of varying viscosities, and oxycholesterins extracted from lanolin. Atreol no. 9 U.S.P. is a light mineral oil. The 685 patients were subjected to a special study in order to establish the efficacy of the emulsified extract. Some of these patients had seasonal pollen asthma and others had both hay fever and asthma. In approximately half of the population (335), the disorder had been present for up to 10 years, and in 218 more for 11 to 20 years.

Symptoms of some type were observed during the ragweed pollen season in 113 of the treated patients, but in only 56 of these could exposure to pollen alone be incriminated. In another 57, an allergen other than pollen, acting alone or cumulatively with ragweed pollen or other allergens or pollens, resulted in symptoms which occurred during the period of ragweed pollination. The symptoms observed occurred in patients who, by intracutaneous and conjunctival tests, had responded with wheals, pseudopodia, and flares to 4 different test levels. They were treated with doses which were based on the arbitrary assumption that the tests indicated the amount of pollen extract to be injected. There was evidence that in the 35 patients treated before May 1, and in the 23 others who took their injections after August 1, symptoms were noted with greater frequency. But no matter when the injection was given, the patients who received smaller doses apparently did not do as well as the others. This may be a result of the small dose injected, or else due to the fact that it takes less exposure to pollen for such patients to respond with symptoms. For the following year, some such patients will receive the same dose (booster principle), some higher doses (higher

dose–higher protection principle), and some, a less denaturalized pollen extract (incomplete protection principle).

The patients who reported for treatment after August 1 could not have been treated at any other time, but for 1959 they will be given injections on dates earlier in the year. The patients treated before May 1 will be given their injections at a later date. The patients allergic to other pollens will be given protection for both. All patients presenting symptoms (without exception) did better than they had done for the previous year, which was one of lesser pollination. But in 113 patients some symptoms, whether mild or subjective, were noted; 56 of these were treated with dexamethasone, and some of the others with mild antihistaminic agents. In the remaining 572 patients treated by means of a single injection of emulsified extract, there were no symptoms whatsoever. From the results seen, it can tentatively be concluded that the emulsion injection treatment represents a major breakthrough in the treatment of human pollinosis.

The Allergic Nature of Essential Hypertension. A. F. Coca. J. Appl. Nutrition 12:69-70 (no. 2) 1959 [Los Angeles].

Coca challenges the definition of the term "allergy" as "an abnormal state caused by the specific interaction of antigen and antibody in a susceptible tissue or organ." The antigen–antibody mechanism was assumed to exist in all conditions of specific sensitivity even when sensitizing antibodies could not be found. It has been adhered to despite the fact that it was disproved by the observation that most adult patients fail to give satisfactory skin reactions to allergenic foods (allergic antibodies being absent). Gay, who was the first to identify essential hypertension as a manifestation of specific sensitivity, emphasized that skin testing, although valuable in inhalant allergy, is not a reliable diagnostic method in food allergy, as there is a high percentage of false-negative and false-positive reactions. He based food testing on Vaughan's "postdigestive leukocyte response," the so-called leukopenic index. Gay also adopted specific tachycardia, the pulse test, as a criterion of an allergic reaction, and later defined it as the method of choice for the study of all manifestations of food allergy, including essential hypertension.

Treatment of Respiratory Acidosis. O. Storstein, T. Elgvin and R. Rokseth. Tidsskr. norske laegefor. 79:667-673 (June 1) 1959 (In Norwegian) [Oslo].

In chronic diffuse pulmonary diseases, destruction of larger amounts of lung tissue and insufficient ventilation of the alveoli will make the lungs unable to renew the blood gases. Anoxemia and hypercapnia result. Anoxemia is, as a rule, the first sign of pulmonary failure. Later the carbon dioxide content in the arterial blood also increases, and respiratory acidosis occurs. The reduced arterial oxygen saturation causes a central cyanosis. In the chronic cases described, the narcotic effect of carbon dioxide becomes evident. The important basic disease is emphysema due to chronic bronchitis, and the acute deficiency is often precipitated by an acute infection. Two of the 6 patients reported on had acute pneumonia; 4 had cor pulmonale. The results of blood gas analyses were decisive for diagnosis and treatment. All the patients were given oxygen, usually by nose catheter. In case of doubt as to the possible harmful effects of oxygen, it was given by nose catheter in a weak stream for half an hour followed by an hour's pause; if no tendency to hypoventilation was seen, the stream was increased.

It is important for the physician to be aware of the possibility of hypoventilation and carbon dioxide narcosis and to be ready to administer some form of artificial respiration in patients with alveolar hypoventilation. Increased carbon dioxide accumulation leads to increasing carbon dioxide narcosis, and the patient dies. If the carbon dioxide excess can be removed by increased lung ventilation and the patient can be brought to a normal carbon dioxide pressure in the arterial blood, his respiratory center will react normally to carbon dioxide stimulus, and he will be free from symptoms for months and years. The disastrous effect of oxygen and morphine is shown in the first case reported; the patient fell into a coma after the combined administration and died within a few hours without being given artificial respiration. Two patients died of cor pulmonale.

Acute Promyelocytic Leukemia: Study on 20 Observations. J. B. Mathé, J. Boulay, B. Céoard and J. Chomé. Schweiz. med. Wchnschr. 89:604-608 (June 6) 1959 (In French) [Basel, Switzerland].

The authors report clinical, hematological, and anatomic observations made during the last 20 years in 20 patients with acute promyelocytic leukemia. The ages of the patients ranged from 15 months to 75 years, but the majority of them were less than 20 years old. The onset of the disease in these patients was sudden, and the course was short. The disease was characterized by the infrequent occurrence of lymph node or spleen enlargement and by the frequency of hemorrhagic manifestations related not only to thrombocytopenia but also to accelerated fibrinolysis. All the patients showed, besides extensive hemorrhagic manifestations, severe anemia resulting in tachycardia, dyspnea, or cardiovascular disturbances. Adenopathies were present in 10 of the 20 patients, and manifestations referable to the bones in 7. Inflammation of the nasopharynx with a fibrinoid

necrotic reaction was present in one patient, and necrosis of the wing of the nose in another. Fever was present in all the patients at the time of admission to the hospital. The results of the examination of the bone marrow were characterized in all the patients by a hyperplasia of promyelocytes associated with a general increase in cells. The patients were treated with cortisone or other steroids, but, except for one patient who had a transient remission, the course of the disease was rapidly progressive, and the patients died. Promyelocytic leukemia and myeloblastic anemia can easily be differentiated by the cytologist, whereas a differential diagnosis between acute promyelocytic leukemia and a certain bone marrow aplasia in which the bone marrow shows an increase in the number of promyelocytes is more difficult to establish. Anatomic lesions found at autopsy are on the basis of promyelocytic hyperplasia, infiltration of the viscera with these cells, and hemorrhagic phenomena.

Further Observations on the Combined Cortisone-Antibiotics Therapy for Infectious Diseases; in Particular, the Therapy with Intravenously Administered Cortisone. R. Scalabrino. Minerva med. 50:1578-1588 (May 23) 1959 (In Italian) [Turin, Italy].

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The author reviews his experience with the combined preparation of hydrocortisone sodium succinate, corticotropin (ACTH), and antibiotics in the treatment of certain infectious diseases. Hydrocortisone and ACTH are administered intravenously. The combined preparation can reduce the mortality rate in the following conditions: certain severe infectious diseases characterized by a high degree of hyperergia and toxicity and accompanied by marked neuroendocrinic stupor; diseases in which there is a considerable degree of involvement of the adrenals, such as the Waterhouse-Friderichsen syndrome, highly acute sepsis in childhood, and the adrenal variety of brucellosis; acute episodes of asthma associated with insufficiency of the right ventricle; cerebral apoplexy; surgical shock and in bilateral adrenalectomy; infections or severe traumatic "stresses" which develop in the course of long-term cortisone therapy; some varieties of blood disease; and the acute phases of rheumatic and collagenous diseases. The combined preparation can also shorten the course and attenuate the toxic effects of sepsis in older persons. An additional advantage in administering hydrocortisone intravenously is to produce immediate effects, whereas those produced by other routes are slower. The author suggests decreasing the dosage of hydrocortisone, although no standard rule can be set regarding the dosage and duration of treatment with the combined preparation.

Epidemic Hemorrhagic Fever Investigation in the T'uliho Area, Inner Mongolia, and Clinical Study of 104 Cases. F. H. Ch'iu, T. C. Hou, P. S. Huang and others. Chinese M. J. 78:515-531 (June) 1959 (In English) [Peking].

During an epidemic outbreak of acute infectious disease in the T'uliho area of Inner Mongolia in 1955, the authors observed 198 patients who had been given a preliminary diagnosis of epidemic hemorrhagic fever. The diagnosis was confirmed in 80 typical and 24 atypical cases that constitute the subjects of this report. Of the typical cases, 68 patients were men and 12 were women; they included all ages, with a predominance of young adults. In 60% of the typical and 75% of the atypical cases the patients were in the 20-to-39-year age bracket. Although the clinical manifestations of this disease vary tremendously, the course of the typical cases was marked by the succession of 5 phases, which are designated, according to signs and symptoms predominating in each, as febrile, hypotensive, oliguric, diuretic, and convalescent. The basic pathological changes in epidemic hemorrhagic fever are extensive damage and dilatation of the capillaries and increased fragility and permeability of the capillary walls, with consequent hemorrhages and plasma transudation, fall of blood pressure, hemoconcentration, and several complicating pathophysiological changes. According to the data collected by the team of specialists who made a coordinated study of the T'uliho outbreak, a virus is possibly the causative agent; wild rodents are the most likely reservoir hosts, and mites the vectors.

No specific treatment has yet been found for epidemic hemorrhagic fever. Antibiotics were administered to the patients in the T'uliho outbreak without any noticeable effect. The general management of the cases reported here consisted of isolation of the patients during the first 10 days of the illness; disinfection of blood and urine specimens; a diet high in carbohydrates and vitamins, low in protein and salt; treatment of the specific symptoms and complications as they occurred in the individual cases. Of the 80 typical cases studied, 71 patients recovered. The main causes of death in the 9 fatal cases were shock, uremia, and acidosis. All the patients with atypical epidemic hemorrhagic fever recovered. Follow-up studies were carried out in 95 cases for 1½ to 2 months after recovery. In 9 patients symptoms of the diuretic phase were still present, and a few patients still suffered from mild headache, dizziness, and weakness. The authors call attention to the need of differentiating epidemic hemorrhagic fever from other acute febrile infections, blood disorders such as hemorrhagic and allergic purpura, and kidney diseases. The differential diagnosis is established by etiological and serologic studies.

Functions of Testes and of Adrenal Cortex in Acute Hepatitis and Cirrhosis of the Liver. H. Voegt and O. Weller. Deutsche med. Wchnschr. **84**:1093-1096 (June 12) 1959 (In German) [Stuttgart, Germany].

Men with cirrhosis of the liver often show signs of androgen deficiency. Not only is there a reduction in body hair, but the external genitalia decrease in size, potency and libido decrease, and gynecomastia may develop. The authors investigated the hormonal and spermatogenic functions of 8 men with cirrhosis of the liver and of 10 men with severe acute hepatitis. The results of the tests in these patients were compared with those in healthy men. It was found that in the presence of acute or chronic damage to the parenchyma of the liver the hormonal and spermatogenic functions of the testes decrease. The reduction is more marked in cirrhosis than in hepatitis. The duration of hepatitis determines the degree of abnormal testicular function. The testicular insufficiency is due to the fact that the anterior pituitary produces less gonadotropin, and this, in turn, is caused by an increase in circulating estrogens and a fall in amino acids and vitamins as a direct result of the liver damage. After the acute hepatitis regresses, the secondary hypogonadism subsides, and the testicular functions return to normal.

Urinary aldosterone excretion is increased to 2 or 3 times the normal value in acute hepatitis and compensated cirrhosis. In decompensated cirrhosis of the liver the urinary aldosterone excretion rises further after the ascites fluid is removed by paracentesis. The concentration of the Porter-Silber chromogens in plasma and urine is greatly reduced in patients with hepatic cirrhosis. In severe acute hepatitis there are no definite abnormalities in the 17-hydroxycorticoids. Functional tests of the adrenal cortex by means of injections of corticotropin (ACTH) indicate that the hypocorticoidism is secondary, that is, it results because the liver disease diminishes the formation of corticotropic hormone.

Primary Carcinoma of Liver. M. Joselevich and Z. Markus. Prensa méd. argent. **46**:173-177 (Jan. 16) 1959 (In Spanish) [Buenos Aires].

Two patients, 77 and 54 years old, respectively, with primary carcinoma of the liver were observed. The symptoms appeared in one 2 months and in the other 3 weeks before hospitalization. Both patients complained of marked weakness, hypochondriasis on the right, epigastric and hemithoracic pain, rapidly progressive hepatomegaly, loss of weight, gastrointestinal disorders, and ascites which was of fibrinous type in one patient and hemorrhagic in the other. In the first patient, the symptoms were those of cirrhosis of the liver with jaundice and fever. A clinical diagnosis of hypertrophic cirrhosis of the liver was made. The disease followed a rapid course with final hepatic coma. The patient died 17 days after hospitalization. An autopsy showed massive primary carcinoma of the liver (originating in the intralobular bile canaliculi) and metastases to the regional lymph nodes and to the kidney. In the second patient, the symptoms were those of a tumoral liver. Puncture biopsy of the liver showed hepatoma. No autopsy was permitted.

The Kidney in Macroglobulinemia of Waldenström. P. Michon, G. Rauber, A. Larcan and F. Streiff. Presse méd. **67**:1267-1270 (June 24) 1959 (In French) [Paris].

The authors studied 7 patients with macroglobulinemia of Waldenström and reviewed 200 cases of this disease cited in the literature. The analysis showed that macroglobulinemia is frequently associated with renal manifestations which are similar in many respects to those observed in patients with multiple myeloma and also in other pathological states, such as cryoglobulinemia and atypical dysproteinemia. Laboratory findings in patients with macroglobulinemia of Waldenström may show mild azotemia, albuminuria, or variable globulinuria, and sometimes Bence-Jones albumosuria indicating subacute nephritis. The similarity in the clinical, biological, anatomic, and physiopathological aspects of these renal anomalies accompanying other major dysglobulinemias suggests that all should be classified in one group, i. e., as dysglobulinemic nephropathies. This new entity should be kept in mind in treating patients exhibiting certain forms of renal insufficiency, and the tests needed to establish the diagnosis should be made.

Kanamycin Treatment of Chronic Bronchitis. F. Hahnemann and I. Gragsted. Ugesk. læger **121**:879-881 (May 28) 1959 (In Danish) [Copenhagen].

Twelve patients with acute flare-up of chronic bronchitis were treated with kanamycin; in most cases a disappearance of Pfeiffer's bacilli was demonstrated, but there was no certain clinical improvement. Like other investigators, the authors found no renal or vestibular injury, but there was injury of the auditory nerve in 3 cases. Kanamycin is considered unsuitable for the treatment of chronic bronchitis, especially in patients with reduced renal function.

SURGERY

Treatment of Tumors of the Parotid. R. Funder. Tidsskr. norske laegefor. **79**:663-666 (June 1) 1959 (In Norwegian) [Oslo].

Salivary gland tumors in the parotid are of considerable interest because of the high frequency of recurrence closely related to inadequately performed primary operation. Between 150 and 200

such tumors occur in Norway annually. They are mainly salivary gland mixed tumors and are regarded as potentially malignant due to their tendency to recurrence and later transition into malignancy. If the entire capsule, which consists of compressed parotid tissue, and a sufficiently large part of normal parotid tissue are not removed together with the tumor, there is danger of recurrence from the capsule. Total parotidectomy would be ideal. Most frequently subtotal parotidectomy is done in the case of benign mixed tumors, with abundant resection at a good distance from the tumor. In malignancy most authors advise radical parotidectomy without regard to the facial nerve. Selective staining of the parotid gland with a methylene blue solution is advantageous. From 1956 to 1959, 22 operations for parotid tumor were performed at the Rikshospital in Oslo. The average duration of the tumors was 6 years—4½ years for the benign tumors and 15 years for the carcinomas. The average age of the patients was 43 years. Women predominated. The tumors were almost twice as frequent on the left side. Local pain was present in the affected area in 7 of the 19 patients with benign tumors. Primary operation was done on 16 patients with benign tumors, and 3 patients were operated on for recurrence after earlier operation, with subtotal parotidectomy in 18 cases and enucleation of the tumor in 1 case. Two of the 3 patients with carcinoma were operated on radically; one patient refused operative treatment.

Surgical Therapy of Strokes. F. R. Denman. Texas J. Med. **55**:563-567 (July) 1959 [Austin].

Denman emphasizes that about 40% of the patients with neurological syndromes simulating stroke have atherosclerotic occlusion of the internal carotid or vertebral arteries in the neck, rather than of the inaccessible intracranial vessels. Cerebral function depends upon a balanced arterial flow through the 4 major cervical trunks and their intracranial branches. Atherosclerotic plaques developing at points of origin of the internal carotid and vertebral arteries narrow the lumen and produce complete occlusion. Thrombo-occlusive disease of the cervical carotid or vertebral arteries is clinically characterized by rapidly or slowly progressive syndromes, featuring blindness and hemianopsia, aphasia, sensory and motor disturbances, convulsion, coma, headaches, memory loss, and confusion or senile dementia. Three clinical syndromes may be recognized: 1. The onset may be explosive and result in the clinical pattern of a fully developed stroke. 2. There may be recurrent episodes of a very transient nature lasting from a few moments to hours and followed by complete or partial recovery for some time before a catastrophic event occurs which produces severe disability or death. 3. A slowly progressive course may be associated with headaches, paresthesias, irritability, memory loss, and mental deterioration.

The occurrence of any of the symptoms should arouse suspicion of caroticovertebral stenosis or occlusion. Inequality of the carotid pulsations is suggestive. Absence of carotid pulsation in the neck indicates occlusion of the common carotid. The presence of a localized systolic murmur over the carotid bifurcation in the absence of a transmitted cardiac murmur indicates a partially occluding lesion. Of special usefulness in diagnosis is the measurement of retinal artery pressures bilaterally. The pressures are low on the side of carotid artery occlusion. Final diagnosis can be made only by angiography or direct exploration. Angiography should be carried out promptly in all patients with symptoms of cerebrovascular insufficiency, to determine the exact anatomic distribution of vascular occlusion, if any, and to assess the status of the collateral circulation.

Since the atheromatous lesions are essentially segmental in nature, they are amenable to arterial reconstructive techniques. In general, 3 methods have been utilized: (1) thrombectomy and thromboendarterectomy; (2) resection and graft or direct union; and (3) bypass procedures by graft or end-to-side union of the external carotid to the internal carotid. All these methods have their application, but because exposure of the distal portion of the internal carotid artery is limited for graft purposes, thromboendarterectomy is frequently most feasible. If surgery is carried out before thrombosis becomes irremovable or brain damage becomes irreversible, excellent results may be obtained, and a significant number of patients will be salvaged.

The Open Correction of Rheumatic Mitral Regurgitation and/or Stenosis with Special Reference to Regurgitation Treated by Posteromedial Annuloplasty Utilizing a Pump-Oxygenator. K. A. Merendino, G. I. Thomas, J. E. Jesseph and others. Ann. Surg. **150**:5-22 (July) 1959 [Philadelphia].

The authors of this report are concerned with the valvular involvement of rheumatic fever, which results in mitral regurgitation, alone or in combination with stenosis. They describe certain relationships of the annulus-valve complex in the competent and the incompetent mitral valve and clinical experiences in patients with mitral regurgitation and/or stenosis secondary to rheumatic fever. They also describe posteromedial annuloplasty, an operative procedure found to be of value in the correction of mitral regurgitation. Having performed the first successful operation utilizing annuloplasty in October, 1956, they report observations on 10 patients: 4 with pure mitral insufficiency; 4 with mitral insufficiency and/or stenosis; and 2 with mitral disease and aortic insufficiency. As regards functional

capacity and clinical status, all 10 patients belonged to either class 3 (the 4 with pure mitral insufficiency) or to class 4 (the remaining 6). The operation was performed under direct vision with the aid of a pump-oxygenator. As experience has been gained and changes in equipment have been made, permitting larger flows during bypass, the postoperative convalescence has become similar to that of patients undergoing blind commissurotomy. The diminution in, and often the total absence of, all murmurs and the reduction in heart size, together with the subjective and objective evidence of improvement, have been most encouraging.

Experience to date indicates that disabling pure mitral regurgitation is accompanied by a large left atrium, a mobile valve without calcium, and a dilated annulus. When the diameter or circumference of the atrioventricular canal is reduced by posteromedial annuloplasty, regurgitation is corrected. The combined lesion of mitral stenosis and regurgitation is characterized by a mild to moderate enlargement of the left atrium, a badly deformed valve with calcium, a shortening of the posterior cusp, and a mild to moderate dilatation of the annulus. After correction of the stenosis by commissurotomy, a limited posteromedial annuloplasty may correct the associated regurgitation. No substitute for valve substance was attempted in this series. The simple maneuver of forcibly elevating the anterior and posterior cusps, grasped by clamps, proved invaluable in identifying the "chordal gate" for commissurotomy.

The authors call attention to maneuvers which tend to lessen the danger of air embolism. Packing the mitral valve area prior to the removal of atrial thrombi appears to be an aid in preventing the systemic embolization of fragmented clots. Thrombi were encountered only in pure mitral stenosis. The mortality of open mitral valve surgery, while high, is approaching the risk of blind commissurotomy in patients of class 4 clinical status. However, the presence of aortic insufficiency, though of secondary hemodynamic importance to the mitral disease, presently constitutes a more serious prognosis. Both of the patients in whom mitral disease was associated with aortic insufficiency died, whereas one each of the other 2 groups of 4 died. Because of the seriousness of even minor degrees of aortic regurgitation, and the inability preoperatively to distinguish between aortic and pulmonic insufficiency, a tie-tape is now routinely placed about the aortic root for control, if needed, in all cases. As this experience represents a learning phase in open surgery of acquired rheumatic valvular disease, it is expected that, with additional experience, errors will be avoided and the risk in future operations will be less.

In an addendum the authors state that, since submission of this paper, 21 patients have been operated on, and this additional experience supports the validity of posteromedial annuloplasty. Best results have been obtained in patients with pure mitral insufficiency; those with mixed stenosis and insufficiency presented the most difficult technical problems.

Analysis of a Case of Constrictive Pericarditis. O. Fustinione, H. Ruggero and I. J. Corsini. Prensa méd. argent. 46:165-169 (Jan. 16) 1959 (In Spanish) [Buenos Aires].

The authors analyze a case of constrictive pericarditis with a 15-year-long course during which ascites constituted the only sign or symptom. Other atypical features in the case were an enlarged heart and an almost normal heart beat. The patient, a 60-year-old man, had been hospitalized 15 years before because of an enlarged abdomen. He had left the hospital one month later, after having undergone 3 abdominal punctures with withdrawal of 8 to 10 liters of fluid at each puncture. Subsequently 3 other punctures had been performed. The patient had been bedridden for several months before rehospitalization. When first seen by the authors, he had been given a diagnosis of hepatic cirrhosis and was scheduled for surgical intervention. All preliminary examinations had been unrevealing. Subsequently laparoscopic findings, as well as the histological examination, suggested the presence of cirrhosis. A new radiogram of the chest, taken in the oblique anterior position, showed an area of calcification around the left ventricle. A radiologic investigation was then carried out in a search for further signs of calcification. Catheterization of the heart showed marked elevation of pressure in the right chambers and reduction in the volume of the systemic circulation. The existence of extensive calcification was confirmed, and the diagnosis of constrictive pericarditis was established.

The patient was treated on a low-salt diet and with mercurial diuretics, digitalis, vitamins, and liver extract; abdominal paracentesis gave temporary relief to the ascites. After 2 months of this treatment, there was improvement of the edema and dyspnea, but the ascites remained unchanged. A surgical intervention was then carried out, the patient being under anesthesia with Pentothal, ether, and intravenously administered Novocain, and with tracheal intubation. The heart was covered with a thickened pericardium; the calcification zones had invaded both ventricles and the openings of both venae cavae. Pericardiectomy was performed, with complete decortication, under direct vision. The surgical intervention was followed by marked general improvement, disappearance of the ascites and edema, decrease in the engorgement of the cervical veins, and increase in the differential blood pressure and the diuresis. The

psychic status was also much improved. The patient was able to walk again, although the exercise caused him some dyspnea and palpitation.

The Triad of Congenital Absence of Aortic Arch (Isthmus Aortae), Patent Ductus Arteriosus and Interventricular Septal Defect—A Trilogy. E. A. Everts-Suárez and C. P. Carson. Ann. Surg. **150**:153-159 (July) 1959 [Philadelphia].

The authors believe that one of the least common, if not rarest, congenital anomalies of the aorta is absence of the arch. They performed an autopsy on a 3-day-old male infant in whom this abnormality was present, accompanied by a defect in the interventricular septum and a patent ductus arteriosus. They also found records of 16 cases of congenital absence of the aortic arch (theirs included), 13 of which were associated with an interventricular septal defect and a patent ductus arteriosus. Regarding the clinical findings, patients with this condition have cyanosis of the lower portion of the body and a normal upper portion. They also show cyanosis on the left, with normal color of the upper right extremity, when the defect occurs distal to the origin of the left common carotid artery but proximal to the origin of the left subclavian artery. These findings, however, have been recorded only occasionally. Some of the symptoms described are dyspnea, cyanosis during feeding or crying, heart murmurs, engorgement of hand veins, weakness and limpness after 24 hours of life, and hepatomegaly.

The possible explanation for the survival of these patients for at least 24 hours, and up to 11 days, appears to be the polycythemia present in infants at birth, the amount of oxygen transported to the tissues being relatively adequate. With the postnatal decrease in the blood count, there is an increase of tissue anoxia which apparently precipitates the death of these infants. The embryologic explanation for the defects is discussed. It is the authors' contention that this entity represents a vascular trilogy not previously discussed as such. It should be brought to the attention of the medical profession and particularly to cardiovascular surgeons.

Atypical Approaches to the Mitral Valve Because of the Impracticability of Approach through the Left Auricular Appendage. C. A. Carlon, A. Jovine and G. Giuliani. Acta chir. ital. **15**:373-389 (May-June) 1959 (In Italian) [Padua, Italy].

The classical approach through the left auricular appendage in performing mitral commissurotomy was not feasible in 21 patients out of more than 600 with mitral stenosis. The approach through the wall of the atrium was made in 15 patients and through the pulmonary veins in 6. Hypoplasia or aplasia of the left auricular appendage, or dilation and thin walls of the atrium, contraindicated the standard approach. A new blade for finger fracture procedure, which was devised by one of the authors, was used with ease and successfully in these operations. The blade has the shape of a nail and is firmly attached to the tip of the finger by a double clamp, being tied securely by 2 long threads with the ends coming out of the glove. The blade has 3 sharp edges, one on the distal side and 2 on the lateral side. This implement makes possible a continuous and uninterrupted procedure in exploring the atrial cavity and mitral orifice and in performing mitral commissurotomy; it thus obviates the necessity of first exploring the mitral orifice with a bare finger, and then reintroducing it with the instrument. The surgeon can precisely resect the commissures by moving the 3 sharp edges of the blade in a saw-cut instead of a rotating fashion. The sharp distal edge cuts through the glove and thus disengages the sharp edges of the blade as soon as the operator presses harder against the mitral orifice. In the series reported, no operative or postoperative death attributable to the technique took place.

A Survey of 102 Patients With Bronchogenic Carcinoma at the Togus Veterans Administration Center. P. F. Lansing, J. Maine M. A. **50**:247-250 and 261 (July) 1959 [Portland].

The author investigated the records of 102 patients with a diagnosis of bronchogenic carcinoma, who were hospitalized between June, 1948, and February, 1957. The average age of the patients was 60 years. The majority of them had noted symptoms, such as cough, weight loss, hemoptysis, chest pain, and chronic pulmonary disease, less than 3 months prior to hospitalization. Of 81 patients in whom the quantity of cigarette smoking was noted, 64 had smoked from 1 to 3 packs a day for 30 to 50 years. Metastases to other organs at the time of initial evaluation were suspected in 10 patients and definitely diagnosed in 27; the condition was present but was missed in 5 patients. Metastases developed during the course of illness in 33 patients; the condition was present but was missed in an additional 3 patients. Jaundice was present during the course of illness in 5 patients.

Forty-one patients whose disease was not considered inoperable were subjected to thoracotomy: on 15 of these pneumonectomy was performed, on 3 lobectomy, and on 14 exploratory thoracotomy alone; tumor removal at thoracotomy, including all lymph nodes, was considered to be complete in 9 patients. Carcinoma was considered inoperable in 45 patients. One patient refused surgery. In 7 patients surgery was inadvisable because of advanced age, severe heart disease, and severe debility. In 8 patients no surgery was undertaken because of poor pulmonary function. Nine patients received

one course of nitrogen mustard. X-ray therapy was given to the majority of patients for palliation; one patient received a cancerocidal dose. Three patients were treated with both nitrogen mustard and x-ray therapy; of these one patient had a superior vena cava compression syndrome.

The time of survival from the first day of hospitalization was less than 3 months for 52 patients. Six of the 15 patients who underwent pneumonectomy survived 2 years. Among the group who received x-ray therapy, there were 2 patients who survived 2 years. Only one of the untreated patients survived 2 years. One patient who had a pneumonectomy with incomplete removal of hilar lymph nodes survived 5 years and is presumably still living. At the conclusion of the survey in February, 1957, there were still 4 living survivors; the time of survival in 6 patients was unknown. The poor survival of this group was considered to be due to the high incidence of metastasis which was present at the time of diagnosis and which also developed during the course of the illness. It is emphasized that the histological type of a cancer is the most important prognostic feature. In this series the survival of patients with epidermoid carcinoma was twice as long as the survival of those with anaplastic carcinoma.

Lung Biopsy for Obscure Pulmonary Lesions. C. C. Craighead. J. Louisiana M. Soc. 111:256-261 (July) 1959 [New Orleans].

The author reports on 3 men and 2 women, between the ages of 30 and 57 years, on whom thoractomy with lung biopsy was performed at the Charity Hospital of Louisiana and the Flint Goodridge Hospital in New Orleans. The operation was accomplished under local or general anesthesia through a small anterior chest incision, with little morbidity and a short stay in the hospital. The pathological processes revealed by the procedure were pulmonary fibrosis, pulmonary metastatic malignancy with impairment of alveolar-capillary-diffusion (so-called alveolar-capillary block syndrome), pulmonary alveolar proteinosis, psittacosis, and aspergillosis. The wide variety of pathological processes observed in the lung is verifiable only by histopathological and biological differentiation, and biopsy of the lung may be necessary to uncover the cause. Studies on the roentgenograms, while usually typical of the disease, overlap in their identities to the point that other aids must be used. Treatment without a diagnosis is often ineffective and may on occasion be dangerous. If an exhaustive survey has failed to yield the underlying pathological process, thoracotomy should be undertaken. Lung biopsy is a dependable diagnostic aid. Two indications for lung biopsy exist: to verify the diagnosis and to establish medicolegal documentation in occupational disease.

Pulmonary Resection for Mineral Oil Granulomas. L. D. Guidry, O. T. Clagett, J. R. McDonald and O. W. Kincaid. Ann. Surg. 150:67-75 (July) 1959 [Philadelphia].

Previous reports on exploratory thoracotomy and pulmonary resection for mineral oil granulomas masquerading as bronchogenic carcinoma attest to perplexities in diagnosis and treatment occasioned by their deceptive appearance. The authors present observations on 11 patients (7 men and 4 women) on whom pulmonary resection was performed for mineral oil granulomas at the Mayo Clinic since 1947. The average age of the patients was 56 years, with a range of 47 to 70 years. Eight patients were evaluated for suspicious-appearing lesions detected on routine roentgenograms of the thorax; roentgenograms in the remainder were obtained for evaluation of symptoms referable to the thorax, namely, chronic cough and night sweats in the first instance, pleuritic pain in the second, and wheezing, pleuritic pain, and mild dyspnea on exertion in the third. Of the entire group, 6 patients gave histories of chronic cough productive of sputum, which the patients attributed to either heavy smoking or sinusitis with postnasal drip. Seven patients used mineral oil (liquid petrolatum) regularly for regulation of the bowels; 2 used it in the form of oily nose drops for chronic sinusitis; and 2 used it for both chronic constipation and sinusitis. A preoperative history of use of mineral oil was elicited in only 4 instances.

Bronchoscopy disclosed abnormalities in only 3 of the 10 patients on whom it was performed. In all cases bronchial secretions, sputum, or bronchial washings were cultured for pathogens and examined for malignant cells. Droplets of mineral oil were detected in the bronchial washings of 1 of the 2 patients who were suspected of having mineral oil granulomatosis. The presence of a pathological process in one or both lungs was evident in the roentgenogram of the thorax in each of the 11 cases. The lesions ranged in size from 1.2 to 8 cm. in diameter. In 4 patients the lesions appeared as rounded, well-circumscribed masses, while in 7 patients they conformed more or less to the segment or segments involved and had poorly defined borders that faded peripherally. The latter presented roentgenographic features often indistinguishable from other types of pneumonitis. The "spun-glass" appearance, described as characteristic of mineral oil pneumonitis or granulomatosis, was present in 3 of the cases. In 4 of the 11 cases the roentgenologic diagnosis was probable bronchogenic carcinoma. In 4 others the disease process was considered most likely to be of an inflammatory nature, and in 3 patients the roentgenologist suggested the possibility of aspiration of lipid. In no patient could the possibility of neoplasm be safely excluded on the basis of the roentgenologic findings.

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Exploratory thoracotomy is advocated for disease indistinguishable from bronchogenic carcinoma, regardless of whether or not mineral oil droplets can be detected in the sputum. Excision is favored for symptomatic or extensive pulmonary involvement when this can be accomplished without excessive sacrifice of normal lung tissue. The establishment of diagnosis should precede any contemplated resective procedure.

Intrathoracic Neurogenic Tumors in Infants and Children: A Study of Forty Cases. O. Schweisguth, J. Mathey, P. Renault and J. P. Binet. Ann. Surg. **150**:29-41 (July) 1959 [Philadelphia].

The 40 pediatric patients reviewed were observed either in the Gustave Roussy Institute, which is a referral hospital for malignant disease, or in the clinic of thoracic surgery of the Hospital Laënnec, a general hospital in Paris. There were slightly more girls than boys (23 compared with 17). The ages of the children ranged from 5 months to 14 years. Neurogenic tumors are subdivided into 2 groups: (1) neurofibromas and schwannomas and (2) tumors of sympathetic origin. The first group of tumors occurs only in adults, so that none of the children had tumors of this type. Of the second group of tumors of sympathetic origin, 15 children had neuroblastomas, 7 had ganglioneuroblastomas, and 18 had ganglioneuromas.

Twelve of the 15 patients with neuroblastomas underwent thoracotomy. The tumor dissection was grossly satisfactory in 7 cases; in 4, tumor fragments were left at the upper pole of the lesion; and in 1 case, only an excision of a biopsy specimen was done. Three patients were not operated on: one had generalized disease; one died after laminectomy; and in the third, the thoracic component in an hourglass tumor disappeared after radiation therapy. Of 4 patients with sufficient postoperative follow-up, only one has survived and is well 3 years later. The 18 children with ganglioneuromas all underwent thoracotomy and tumor excision. The results were uniformly successful. Postoperative complications were absent, with the exception of the development of a chylothorax in one child, who recovered completely.

Diverse treatments were employed in the 7 children with ganglioneuroblastomas. One patient was operated on between 2 courses of x-ray therapy and is in good health 15 months after the initial treatment. Another child underwent surgery after 22 days of preoperative irradiation; this patient is doing well 11 months later. Four children had tumor surgery without any x-ray therapy, and of these, one patient had a local recurrence which was not radiosensitive. A second operation necessitated a pneumonectomy. Histological examination revealed anaplastic neuroblastoma. Two patients operated on recently have had postoperative irradiation. The malignant potential of the neuroblastic component in these tumors would seem to be best managed by both surgery and radiation.

The authors advise caution in evaluating the treatment of tumors of sympathetic origin in children. They do not regard their therapeutic procedures as necessarily the best. They advise surgery alone for neuroblastomas in infants under 2 years of age and for all children with ganglioneuromas. Postoperative roentgen-ray therapy is recommended for ganglioneuroblastomas and neuroblastomas in children over 2 years of age.

Surgical Treatment of Thrombotic Occlusion of Aorta and Iliac Arteries: The Leriche Syndrome. J. M. Erskine, F. L. Gerbode, S. W. French III and R. M. Hood. A. M. A. Arch. Surg. **79**:85-93 (july) 1959 [Chicago].

The syndrome resulting from the arteriosclerotic obliteration of the lower abdominal aorta is known as the Leriche syndrome, because it was first described by Leriche in 1923. A direct surgical attack on the obliterative process in the form of thromboendarterectomy was first carried out by dos Santos in 1946. Because the surgical treatment is still in the developmental stage, the authors review their observations on 33 patients treated surgically during the period from 1953 through 1957. All the patients had intermittent claudication, but the location of the pain in some persons was more widespread than in others. All had pain in the lower legs, and 94% had pain in the thighs and hips as well; only 48% experienced pain in the lower-back area, and in 6% the pain was unilateral. The distance the patient was able to walk before claudication appeared gradually diminished. Another complaint frequent among male patients was inability to sustain an erection.

The femoral pulses were absent or were very weak in the 33 patients, and the more distal pulses were absent. There was little or no atrophy or color change in the lower legs and feet, and the feet might not even feel particularly cold. Roentgenoscopy usually revealed calcification in the abdominal vessels. Aortograms did not seem to be essential in making the diagnosis or in planning the therapy, but they might be required in special circumstances. The block was complete in most of the patients; it often extended from just below the renal vessels to just above the bifurcation of the common iliac arteries. If the block was limited in extent, a thromboendarterectomy was sometimes carried out; but in the majority of cases a resection with grafting was performed. A bilateral sympathectomy was usually added. The operative mortality in the series reported was 3%, and the results were highly satisfactory, through the follow-up period, in more than 90% of the patients, from both the objective and the subjective point of view.

Late Results After Total Gastrectomy for High Gastric Carcinoma. N. Stensrud. Ann. Surg. **150**:63-66 (July) 1959 [Philadelphia].

Total gastrectomy was performed on 160 patients for carcinoma of the stomach at the Rikshospital in Oslo during the period from January, 1947, to February, 1952. The operative technique employed was resection of the stomach, with all surrounding lymph nodes, and of the spleen, followed by esophagojejunostomy. Esophagoduodenostomy was performed in only 2 cases. The pancreas was partially resected in 50% of the cases. Special emphasis was placed on careful dissection of the lymph nodes around the celiac axis. A follow-up of the material was made 2 years ago. Seventeen patients (4 women and 13 men) had lived for 3 years after the operation; the rest were dead. The small group of 17 (10.6%) who had survived for more than 3 years after the first investigation have now been reexamined: 16 of them are still alive; one patient died 6 years after the operation, presumably of cancer. While nearly 90% of the 160 patients died within 3 years after the operation, the prognosis for those surviving more than 3 years is good. Pernicious anemia has developed in all the survivors, but apart from this condition and a moderate dyspepsia, the majority are living an active life, with relatively minor discomforts.

Acute Appendicitis: An Analysis of 1,662 Consecutive Cases. J. R. Babcock and W. M. McKinley. Ann. Surg. **150**:131-141 (July) 1959 [Philadelphia].

The authors evaluate observations on all patients with appendicitis who were treated at the Geisinger Memorial Hospital and Foss Clinic, Danville, Pa., from 1936 to 1955. Patients in whom appendical inflammation was present but was not the primary pathological process were excluded. Thus, some patients with perforating neoplasms of the appendix or adjacent intestine, ileocolic intussusception, strangulated hernia, and pelvic infection were not considered. The records of 1,662 patients were analyzed. The group included 3 children, between 13 and 24 months of age, but none less than one year old. Seven patients ranged in age from 80 to 89 years. Analysis of the case records with regard to the duration of symptoms revealed that, of the 397 patients admitted 12 hours or less after onset, only 15 had appendical perforation. When the duration of symptoms was considered in respect to mortality, it was found that no deaths related to infection occurred in patients admitted within 12 hours from the time of onset of symptoms. Patients found to have perforation were admitted from 25 to 48 hours after onset of symptoms, and those who ultimately died of perforation were admitted even later. When the condition of the appendixes found at operation was compared in the 4 successive 5-year periods, it was found that the proportion of appendixes which were either intact or perforated was stable, the percentages of intact appendixes ranging from 77 to 72%.

All the patients were operated on irrespective of possible perforation. Antibacterial agents were first used in 1938. During the first 5-year period 9.5% of the patients received sulfonamide preparations. Penicillin was first used in 1944 (during the second 5-year period), but at first it was given in conjunction with the sulfonamides. Not until the following year did penicillin become the principal antibacterial agent in patients with appendicitis. During the third and fourth 5-year periods streptomycin and the broad-spectrum antibiotics were used more frequently. During the fourth period (1951-1955) 65% of the patients with appendicitis received various antibacterial agents. More than 50% of those who received such treatments had intact appendixes.

Thirty-five of the 1,662 patients died, a gross mortality of 2.1%, but since 4 of these patients were not operated on, the mortality of operated cases was 1.9%. Twenty-six of the 35 deaths were due to peritonitis. Although the refinement and appropriate use of adjuncts, such as intestinal intubation, blood and fluid replacement, and improvements in anesthesia, are noteworthy, the authors feel that the use of antibiotics—penicillin, streptomycin, and the broad-spectrum agents—during the last decade of the study was of major importance, being the principal cause for the marked reduction of morbidity and the near elimination of the mortality of appendicitis.

Sliding Inguinal Hernia in Female Infants. S. L. Gans. A. M. A. Arch. Surg. **79**:109-113 (July) 1959 [Chicago].

Among 400 infants and children with 516 inguinal hernias (bilateral in 116), there were 68 girls with 90 hernias. Nineteen of these female patients had sliding inguinal hernias, which indicates that this condition is relatively common. Seventeen of the 19 patients were less than 4 months of age; one was 9 months old; and one returned at the age of 3½ years with a sliding hernia on the left side, after having had an incarcerated sliding hernia repaired on the right at the age of 6 weeks. In the majority of the cases there was no complaint. A mass was palpated in the groin or labium majus by the mother or by the pediatrician during a routine examination. The asymptomatic mass varied in size from 1 to 2.5 cm. in diameter; it was always somewhat movable, and occasionally reducible. In other instances the infant was irritable, occasionally drawing up its legs as if in pain, and the mass was somewhat tender to palpation. In 2 instances

there was severe incarceration, with swelling, tenderness, pain, distention, vomiting, fever, and dehydration. The condition must be differentiated from inguinal lymphadenopathy, hydrocele of the canal of Nuck, and male pseudohermaphroditism.

At surgery it has been demonstrated that the fallopian tube and the adjoining part of the broad ligament make up at least a portion of the hernia-sac wall. Usually the ovary is also included, and occasionally a portion of the uterus or the entire supracervical part of the uterus. In most instances the organs involved are normal. The principle involved in surgical treatment is the same as that involved in treating all infant hernias—complete removal and high ligation of the hernia sac. It is the contention of the author that this cannot be done without special handling of the sliding portion of the sac. He makes a 3-cm. transverse incision through the skin and subcutaneous tissues of the lateral portion of the suprapubic crease. The external oblique aponeurosis is incised in the direction of its fibers and retracted, carefully preserving the ilioinguinal nerve. The hernia sac is demonstrated, dissected out, and carefully opened in an area away from the sliding elements. The sac is then incised on each side of the sliding element down to the neck. After hemostasis is secured in the edges, the tongue of the sac, with the sliding element, is tucked through the internal ring into the peritoneal cavity. A silk suture is then placed through the cut edges of the sac, making its circumference complete again. The sac can now be handled in the usual fashion by high ligation and amputation. The author discusses the embryologic background of the anomaly.

Partial Nephrectomy in the Treatment of Renal Tuberculosis. B. di Bello. Acta chir. ital. **15**:335-371 (May-June) 1959 (In Italian) [Padua, Italy].

Partial nephrectomy is a useful surgical procedure in selected instances of renal tuberculosis. The author discusses this treatment in 2 patients. One patient, a 17-year-old girl, with a family history of tuberculosis, had a tuberculous process in the right lung 3 months before being hospitalized for renal tuberculosis. The pulmonary process was arrested by medical treatment. Pollakiuria and painful urination were the symptoms of the involved kidney. The intravenous urographic examination revealed the presence of a small tuberculous cavity in the superior end of the right kidney. The diagnosis was confirmed by examination of the material of the subsequent partial nephrectomy (superior end). A combined treatment with isonicotinic acid hydrazide and streptomycin preceded and followed the surgical therapy. A dose of streptomycin was administered topically during the operation. Symptoms of the renal tuberculous process recurred after 6 postoperative months of apparent well-being, which necessitated performance of total unilateral nephrectomy.

The second patient, a 48-year-old man, had pain in the right side of the lumbar region, painful urination, occasional hematuria, and pollakiuria 2 months before hospitalization. The presence of a calculus in an upper calyx of the right kidney was established on roentgenologic examination. The patient underwent partial nephrectomy of the superior pole of the right kidney. The microscopic findings of the resected material demonstrated renal tuberculosis. Streptomycin was given to this patient until discharged. He was well on follow-up inspection a year after the operation.

Myocardial Nutrition After Ivalon Sponge Operation: The Return of a 400 Million Year Old System. A. Vineberg, T. Deliyannis and G. Pablo. Canad. M. A. J. **80**:948-958 (June 15) 1959 [Toronto].

The use of Ivalon sponge to relieve myocardial ischemia caused by narrowing or occlusion of the coronary artery has raised some strange questions. Is it possible to turn the mammalian heart back into a primitive heart capable of surviving without coronary arteries? Such a primitive heart is to be found in the hagfish, which has no coronary arteries but receives its nutrition directly from the ventricular lumen, i. e., via channels which originate in the lumina of the heart to enter the heart wall through channels between bundles of muscle fibers. A spongework of vascular spaces nourishes the primitive myocardial fibers by direct contact. Does the mammalian myocardial fiber inherit a 400-million-year-old memory so that, given a proper stimulus, it likewise can take its nutrition directly from the ventricular cavity by loosening its own compact structure to one which is more trabecular and by opening up long-unused channels connecting the ventricular cavity to the interior of the heart wall?

These and other questions are being investigated by the authors in the department of experimental surgery, McGill University, and the department of cardiac surgery, Royal Victoria Hospital, Montreal, Canada. Several years ago, the senior author suggested that perhaps one could supply a framework between the myocardium and pericardium through which hundreds of small vessels could grow. Perhaps something with small canaliculi might be of help. After studies had been made with coral formations and marine sponges, it was suggested that Ivalon sponge, an inert substance, would offer an ideal framework to guide the growth of blood vessels from pericardium to myocardium. In order to obtain the proper conditions for such a growth of vessels, at least 3 factors had to be fulfilled: (1) myocardial ischemia had to be created; (2) the

serous lining of the fibrous pericardium and the epicardial covering of the left ventricle had to be removed; and (3) the Ivalon sponge sheet had to be sufficiently thin to permit blood vessels to bridge the gap between the denuded pericardium and the heart muscle. To produce myocardial ischemia, ameroid constrictors were placed around the origins of the anterior descending and circumflex branches of the left coronary artery. (Ameroid is a water-absorbing, casein-like material.) A total of 54 animals were operated on. Of these, 25 were control animals and 29 were treated. After excluding animals with complications, 20 control animals and 22 treated with Ivalon sponge were studied. All but two of the control animals died within 18.8 days, all apparently from myocardial ischemia. Of the animals treated with Ivalon sponge, 19 survived for 3 months or longer.

It was found that, when the epicardium of the left ventricle is removed and a thin layer of Ivalon sponge placed directly on the bared myocardial muscle, blood vessels from the fibrous pericardium grow through the sponge into the heart muscle. Further, there is evidence to suggest that, in addition to affording a scaffolding for blood vessel growth from outside into the heart muscle, the Ivalon sponge tends to open up long-forgotten arterioluminal and perhaps myocardiosinusoidal luminal vessels. In this way a heart treated with Ivalon sponge may theoretically receive its nutrition both from outside and from inside the ventricular chamber. The size and frequency of these openings from the ventricular lumen into the heart wall makes one wonder whether these hearts have actually changed into a 400-million-year-old prehistoric type of heart which lives without coronary arteries and receives its nutrition from the heart chambers.

In an addendum to this paper the authors state that the Ivalon sponge operation alone, or together with mammary artery implantation, has been used in 14 patients. Details of the clinical results are being compiled.

The Relation Between the Nasal-Staphylococcal-Carrier State and the Incidence of Postoperative Complications. H. J. Weinstein. New England J. Med. **260**:1303-1308 (June 25) 1959 [Boston].

The author observed 125 patients, most of whom received chest surgery. The patients had been hospitalized for an average period of 4 months before the operation, except those in whom other conditions, such as cancer, were suspected and in whom surgery was done at once. The patients were not given antibiotics unless a clear-cut sepsis was present. All patients with nose cultures positive for hemolytic, coagulase-positive Staphylococcus aureus were subjected to topical application to the anterior nares of a bacitracin-neomycin ointment 3 times a day. The treatment was usually begun about 4 days before the operation and continued through the immediate postsurgical period, being discontinued on the 4th or 5th postoperative day.

Thirty-four per cent of the 125 patients undergoing elective surgery had hemolytic, coagulase-positive Staphylococcus aureus recovered from cultures of their noses. Forty-three per cent of those with positive nose cultures had complications of surgery, as compared to 26% of those with negative cultures. Among those with positive cultures 83% of the complications were infected, whereas 40% were infected in the group with negative cultures. The over-all surgical failure rate was 23.3% in those with positive and 7.3% in those with negative nose cultures. It is pointed out that it has always been good practice to postpone elective surgery on patients manifesting infectious processes. This good practice should be extended to include patients who are potentially infected, in addition to those who are clinically infected.

The Surgical Treatment of Endocardial Cushion Defects. D. C. McGoon, J. W. DuShane and J. W. Kirklin. Surgery **46**:185-196 (July) 1959 [St. Louis].

The embryonic division of the heart into its 4 chambers involves the growth and final convergence of the atrial septum, the ventricular septum, and the endocardial cushions. A variety of congenital cardiac anomalies, involving the atrioventricular valves and the adjacent portions of the interatrial and interventricular septums, is believed to result from the defective development of the endocardial cushions. The terminology applied to these anomalies has evolved through an increasing understanding of their anatomy and embryology, a process which left behind a confusing nomenclature. Only after recognition of the fact that the "persistent ostium primum atrial septal defect" is characteristically accompanied by deformity of the atrioventricular valves was it realized that the name was not adequately descriptive. Some investigators have postulated 14 theoretically possible combinations of defects. It thus has become necessary to use a more comprehensive title to encompass all variants of this expanded group of lesions. The term "endocardial cushion defects," previously proposed by Watkins and Gross, seems appropriate for this purpose, since the basic abnormality common to each of the variants results from defective development of the endocardial cushions.

The case records of all patients in whom cardiac defects of this type were found at open-heart operations performed at the Mayo Clinic have been reviewed. There were 54 such patients, the first having been operated on in March, 1955, and the others between that date and Jan. 1, 1959. From a practical clinical standpoint, it seemed best to classify endocardial cushion defects into 4 groups. There is no objection to the anatomic classification

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of certain defects in a transitional or intermediate group between the partial and the complete form of the common atrioventricular canal; however, these transitional varieties typically function as either partial or complete forms of the defect, and hence it has seemed impractical in this study of surgical patients to attempt to separate such intermediate forms.

Included in the group of 54 patients are examples of the 4 varieties of endocardial cushion defects, namely, partial atrioventricular canal, complete atrioventricular canal, ventricular septal defect with cleft atrioventricular valves, and common atrium. A marked difference was apparent between the partial and the complete form of this defect, both in the natural history and in the results of surgical treatment. For the partial form, surgical repair was highly successful and safe, even to a degree comparable to the repair of the ordinary atrial septal defect. For the complete form, operative mortality was very high. The 2 examples of ventricular septal defect with cleft atrioventricular valves are believed to be the first of this type which have been reported. Certain techniques and principles for the repair of these lesions have become apparent during this experience. Of particular importance is the requirement that the function of the atrioventricular valves be restored by the repair to as nearly normal as is possible.

Treatment of Esophageal Varices by Partial Esophagogastrectomy and Interposed Jejunal Segment. D. V. Habif. Surgery **46**:212-237 (July) 1959 [St. Louis].

This report deals with the author's experience in trying to achieve a permanent cure from varix hemorrhage for patients who cannot have a portacaval shunt, and the present plan of operative treatment evolved from this experience. From August, 1948, through July, 1951, 7 patients were operated on. The operation was an almost total gastrectomy, leaving 2 cm. of stomach on the greater and lesser curvature sides below the esophagogastric junction. Two patients have had no bleeding to date, but 5 had subsequent bleeding and 3 of these had a successful lower one-third esophagectomy. From December, 1952, through October, 1958, 21 patients were operated on. The operation was a partial esophagogastrectomy of the lower third of the esophagus and the upper 5 cm. of stomach. Seventeen patients had extrahepatic block, and 4 had cirrhosis. There were 4 deaths, and among the 17 survivors, 2 had further hemorrhage. Nineteen of the 21 patients had reconstruction with an interposed isolated segment of jejunum —7 with an isolated vascular pedicle where the intestine was supplied through a single artery and vein to the arcuate, and 12 without interruption of the arcuate vessels distally.

The following plan of treatment has been evolved for the nonemergency definite treatment of patients with portal hypertension and recurrent bleeding from esophageal varices: (1) a portacaval shunt of some type; (2) transesophageal ligation of varices for children under the age of 7 or 8 years, who have frequent episodes of hematemesis and have an intact spleen where the splenic vein is as yet too small for a splenorenal shunt and no other shunt is possible or successful; it is a temporary measure, however, since a splenorenal shunt may be attempted at a later date; (3) partial esophagogastrectomy with interposition of a jejunal segment for patients who are "shunt failures" or cannot have a shunt; and (4) resection of the midesophagus for those patients who have bleeding from residual varices after lower one-third esophagectomy.

Metastases of the Internal Mammary Chain of Lymph Nodes in Patients with Mammary Carcinoma. G. Silini and P. Metalli. Minerva chir. **14**:455-464 (May 15) 1959 (In Italian) [Turin, Italy].

The internal mammary chain of lymph nodes was early involved in the metastatic process of mammary carcinoma in 25 patients who underwent the classical radical operation on the breast and clearing of the homolateral parasternal region. Microscopic examination of the removed material revealed involvement of the internal mammary chain of lymph nodes in 10 patients (40%) and of the axillary lymph nodes in 21 (84%). The axillary lymph nodes were involved in all instances in which there was metastasis of the internal mammary chain of lymph nodes. If metastases of the axillary lymph nodes were not present, the internal mammary chain of lymph nodes was not involved either. The size of the primary lesion was about 3.3 cm. in diameter if the axillary lymph nodes were involved and was under 2 cm. if they were not involved. The size of the primary lesion was about 3.6 cm. in diameter if the internal mammary chain of lymph nodes was involved and it was about 2.7 cm. if it was not involved. Of 10 instances of metastases of the internal mammary chain of lymph nodes, 6 were adenocarcinomas; 2, hard carcinomas; 1, scirrhous carcinoma; and 1, vegetating carcinoma. The same varieties of carcinoma were found in the metastatic material obtained from the axillary region. Malignant epithelial cells were found in lymphatic tissue around the arterial vessels in 2 patients after they had been cleared for involvement of the internal mammary chain of lymph nodes. This incidence suggests the necessity of a thorough inspection of the vascular fasciae between the lymph nodes before making the diagnosis of noninvolvement of the adjacent areas.

From the early invasion of the internal mammary chain of lymph nodes, it could be interpreted that there exists a certain relationship between the

stage of the neoplastic disease and the involvement of the internal mammary chain. Nothing can be said about a possible correlation between the location of the primary lesion and the histological variety and frequency of metastases in the peristernal region.

Single or Double Segments of the Lung Occupying a Hemithorax: Clinical and Physiologic Evaluation. R. H. Overholt, E. A. Gaensler and J. A. Bougas. New England J. Med. **261**:10-18 (July 2) 1959 [Boston].

Disease may destroy all but 1 or 2 segments of a lung. Often surgery is imperative, with a choice between pneumonectomy and conservation of the single or double segment. If there is disease on the opposite side, preservation of functioning lung tissue becomes important. Although lobectomy combined with segmental resection theoretically provides maximal preservation of function, it may present more formidable technical problems and postoperative hazards than pneumonectomy. Such added effort and risk can be justified only if it can be shown that the 1 or 2 residual segments contribute significantly toward the pulmonary economy. Because no data are available from the literature concerning clinical course and pulmonary function with single-segment or double-segment occupancy in a hemithorax, a late postoperative study of such patients was made. On 14 occasions during the past 12 years the opportunity presented for studying patients with 1 or 2 segments remaining within a hemithorax. All had undergone extensive pulmonary resection on one or both sides for treatment of severe bronchiectasis that had produced disabling symptoms.

Clinical and physiological data obtained in studies on these patients leave no doubt that, in most cases, 1 or 2 healthy residual segments on one side may contribute greatly to over-all functional capacity. In patients with intact and presumably healthy opposite lungs, preservation of 1 or 2 segments resulted in greater over-all function than is ever seen after pneumonectomy. A single segment was found to contribute as much as 23%, and 2 segments as much as 33% to total oxygen uptake at rest. In addition, the residual lung tissue prevented, or greatly reduced, mediastinal shift to the side of operation. With contralateral inoperable bronchiectasis, the share of function of the remaining segments did not increase as expected, presumably because they also were involved by disease, which was diffuse throughout all parts of the lung. After extensive contralateral resection the 1 or 2 remaining segments made a larger contribution to the greatly taxed respiratory economy and, in extreme cases, were responsible for nearly half the total respiratory work. In nearly all cases with functioning residual segments, their ventilatory contribution was relatively greater than their participation in oxygen uptake. This unfavorable ventilation–perfusion ratio may have been disturbing in one case. The functional contribution of the single and double segments in patients with well opposite lungs was greater than that predicted from theoretical consideration. In 4 cases with extensive disease or resection on the opposite side, the residual lung tissue was probably necessary for life.

Traumatic Mediastinitis and Thrombosis of the Superior Vena Cava. J. E. Rodo. Medicina **19**:17-27 (Feb.) 1959 (In Spanish) [Buenos Aires].

Thrombosis of the superior vena cava, due to mediastinitis from direct trauma, is rare. The signs and symptoms depend on the velocity at which obstruction of the superior vena cava has taken place and the acuteness of the obstruction. The characteristic signs and symptoms are: (1) edema and cyanosis of the face, neck, arms, and hands (which increase when the patient is lying down and diminish in the standing position); (2) venous hypertension in the arms and normal venous tension in the legs; (3) development of varicose veins in the anterior and lateral surfaces of the thorax; and (4) establishment of deep collateral venous circulation and dyspnea. The treatment consists of thoracotomy with removal of cicatricial tissue for liberation of the newly formed collateral vessels.

A 32-year-old man reported for consultation with typical signs and symptoms of obstruction of the superior vena cava one year after the occurrence of trauma to the chest. The results of phlebographies confirmed the clinical diagnosis of caval obstruction. The operation consisted of median sternotomy and removal of fibrous tissue for liberation of the superior vena cava. Histological examination of the removed tissue showed chronic inflammation. The postoperative period was uneventful, and the patient was discharged in a satisfactory condition. A follow-up for 6 years has shown that he has been in normal health since the operation. The roentgenograms of the chest have been normal. Moreover, the venous hypertension in the arms has diminished (in comparison with the condition before the operation); this fact is probably due to improvement of the collateral circulation after the operation.

Results of the Treatment of Postoperative Peptic Ulcer by Vagotomy. L. Ruyters, P. Maquet and F. Orban. Acta gastro-enterol. Belg. **22**:187-211 (April) 1959 (In French) [Brussels].

The authors present the results obtained by transthoracic bilateral vagotomy in 14 patients with postoperative peptic ulcer. The original operation consisted of gastrectomy in 11 cases and of gastrojejunostomy in the other 3. The period of follow-up after vagotomy ranged from 5 months to 6½ years.

All the patients presented symptoms suggesting ulcer: epigastric or left hypochondriac pain, in rhythm with meals and relieved by alkalines at first but later becoming severe and unresponsive to the ingestion of food or alkalines; significant gastric hemorrhage at times; undernourishment due to fear of pain or anorexia; and inability to work normally.

The results of vagotomy were excellent in 8 patients with peptic ulcer following gastrectomy: clinical improvement was accompanied, first, by a reduction in, and, later, by the disappearance of, the roentgenologic picture of ulcer. Good but less perfect results were obtained in the patients with gastrojejunitis and hyperacidity; one continued to have mild dyspepsia of a gastritic type, and all showed hyperacidity in the fasting state. The standard procedure in the patients who had undergone gastroenterostomy would have been a degastrogastrectomy. Two of them, however, were so old that their ability to withstand such a serious operation was uncertain. Vagotomy was, therefore, given a trial and was followed in each case by clinical and radiologic cure. The third patient in this group had an extremely large ulcer niche, and vagotomy was decided on as a first step to reduce inflammatory phenomena. The results were so satisfactory that no further operation was needed, and the patient has remained well for 6 years.

Vagotomy thus appears to be an excellent procedure for patients with postoperative peptic ulcer. It entails a minimum of operative risk and may produce a complete cure. It is not an absolute safeguard against recurrence, but the same may be said of reoperations on the stomach, which are not always effective and which may lead to total gastrectomy.

NEUROLOGY & PSYCHIATRY

Cerebral Paragonimiasis: A Report of Forty-Seven Cases. S. K. Kim. A. M. A. Arch. Neurol. 1:30-37 (July) 1959 [Chicago].

The habit of eating raw crabs and other crustaceans is responsible for infection by the lung fluke, Paragonimus westermani. This habit is prevalent in Far Eastern countries, where paragonimiasis is endemic. Since Otani, of Japan, first called attention to the high incidence of cerebral involvement in 1887, there have been many case reports based on postmortem examination, but only 21 instances of cerebral paragonimiasis have been demonstrated surgically. The present paper is based upon the cases of 47 persons examined by the author; the diagnosis was made at the time of operation in 45 cases and at autopsy in 2. Almost all the patients gave a history of eating raw and poorly cooked crab and/or crayfish. Some apparently were infected through raw fish or impure water.

By far the commonest initial manifestation of cerebral paragonimiasis was a seizure (31 cases). The remainder of the patients, with 2 exceptions, had a seizure at some time in their course. The type of seizure seemed to depend upon the localization of the intracranial lesion. The majority of the patients gave a history of some type of paroxysmal minor impairment of neurological function, which after a time developed into frank grand mal attacks. Patients with multiple cysts frequently had several types of convulsive episodes. Sudden hemiplegia was the first symptom in 6 patients. In 6 other patients the predominant symptoms were those of chronic meningitis, with headache, stiff neck, vomiting, and fever. Severe headache associated with papilledema was noted in 7 patients, but others complained of mild headache. Fever was noted in 18 patients. Feeblemindedness was frequent.

The diagnosis of cerebral paragonimiasis is usually suggested by hemoptysis in a young person (generally a peasant) who lives in an Oriental country where the disease is endemic and who has had some mental impairment and symptoms of cerebral involvement, such as convulsions or a stroke. The finding of ova or a fluke in the sputum or stool would confirm the diagnosis; the complement-fixation test might help. Eosinophilia in the blood is suggestive of paragonimiasis in an Oriental. Roentgenograms of the skull and chest usually show typical lesions. In treatment, emetine and antimony sodium tartrate (Stibnal) were given to 9 patients in this series, and resulted in a discharge of ruptured ova in the sputum. The cerebral symptoms were not improved.

The author lists criteria favoring the presence of a localized process suitable for surgical excision, as well as criteria indicating multiple or diffuse lesions not suitable for surgical treatment. Surgical resection of the cerebral abscess often relieved the convulsive episodes, although some patients continued to have less frequent minor seizures. If the brain abscess was not surgically removed, even though it became calcified or well encapsulated, generalized seizures persisted for long periods. While in patients with localized lesions surgical excision offers a good chance for relief of the epilepsy and arrest of the cerebral disease, in those with diffuse and multiple lesions surgery has little to offer.

Cerebral Vasospasm in Angiography for Intracranial Aneurysms: Incidence and Significance in One Hundred Consecutive Angiograms. T. M. Fletcher, J. M. Taveras and J. L. Pool. A. M. A. Arch. Neurol. 1:38-47 (July) 1959 [Chicago].

This study is concerned with the clinical implications of cerebral vasospasm as determined by angiography. The authors believe that spasm of

the internal carotid artery or its major branches is a common accompaniment of ruptured intracranial aneurysm and that the patient's clinical course may be dependent to a large degree upon the presence, extent, and duration of this spasm. It may result in localized or generalized insufficiency of the cerebral circulation, thereby producing ischemia of varying degrees in the involved areas of distribution. Recognition of the occurrence of the spasm may be of considerable value to the neurologist and the neurosurgeon alike, particularly as to prognosis and as a guide to management, and occasionally in diagnosis or localization. The authors designate as spasm a narrowing of the lumen of a vessel beyond what they consider a normal anatomic variant.

Up to 1957 it was the policy at the Neurological Institute of New York to carry out angiography after the patient's clinical condition had become stable and there were no signs of continued or new bleeding. In only one-tenth of the patients in this series was angiography carried out before the 5th day. It was not thought that angiography altered the course of the disease except in 4 cases, in which the patient's condition became worse after the procedure, and only 2 of these demonstrated spasm. Angiography was performed by means of percutaneous puncture of the common carotid artery, and serial films were made by identical roentgenologic techniques. For the purposes of this study the cerebral angiograms of 100 consecutive patients with intracranial aneurysm were reviewed and correlated with the clinical history, findings, and course. Cerebral vasospasm did not occur in major cerebral arteries having clear-cut evidence of arteriosclerotic changes, presumably because such vessels are no longer capable of spasm. The type of vasospasm under discussion usually occurred within 3 weeks of aneurysmal rupture and was usually associated with bloody cerebrospinal fluid.

Recognition of the presence of vasospasm is of particular value as a guide to prognosis and management, and occasionally is of localizing value when an aneurysm fails to fill with contrast material or when multiple aneurysms are present. The presence of gross blood as a local irritant is one explanation for the production of spasm. However, since spasm may occur in the absence of blood, and is usually absent on the opposite side from a bleeding aneurysm, there may be an additional factor in the production and maintenance of cerebral vasospasm. This could be a local muscle or nerve reflex effect caused by the distention or rupture of the aneurysm. The occurrence of vasospasm and serious resultant neurological signs may be delayed for several days after subarachnoid hemorrhage, indicating the advisability of prompt surgical treatment of ruptured intracranial aneurysms.

Chlorpromazine—Four Years Later. W. Tuteur, R. Stiller and J. Glotzer. Illinois M. J. 116:9-12 (July) 1959 [Chicago].

The authors report on a 4-year continued survey of 822 psychiatric female patients treated with chlorpromazine. The patients, the largest age sector of whom was between 41 and 50 years, presented symptoms of incontinence, combativeness, destructiveness, noisiness, and tendency to undress; the majority of them had been hospitalized for from 1 to 15 years. Seventy-seven of the 258 patients who were conditionally discharged during the 4-year period, to be followed by systematic treatment with chlorpromazine, have returned, 26 of them for relapses which occurred while taking the drug diligently. The doses of chlorpromazine given to inpatients ranged from 100 to 1,200 mg. orally, or 50 to 150 mg. intramuscularly, per day; doses for outpatients varied from 50 to 800 mg. orally. During the 4-year survey 6 patients out of a total of 181 discharged patients have been away from the institution for more than 3½ years, 36 for 3 to 3½ years, 24 for 31 to 36 months, and 34 for more than 2 years. Fifty-five of the 181 patients remaining outside the institution have found gainful employment. Placebos were given to 72 discharged patients, and 43 suffered from relapses, showing symptoms similar to their pretreatment clinical picture and indicating that they might need drug treatment for an indefinite time. Five of these had to be rehospitalized, but the others showed sufficient improvement within several days after treatment with chlorpromazine had been restarted.

The authors point out that since the introduction of chlorpromazine it has been possible to remove 118 beds from the overcrowded cottages of the institution where the study was made. These same cottages used to discharge only 2 to 6 patients a year before the introduction of this beneficial drug.

Virus Infections of the Central Nervous System Transmitted by Arthropods in Europe. H. Moritsch. Schweiz. med. Wchnschr. 89:683-685 (June 27) 1959 (In German) [Basel, Switzerland].

Among the epidemic virus diseases transmitted by arthropods, such as western equine encephalomyelitis and hemorrhagic or Q fever, spring-meningoencephalitis represents the most important infection of the central nervous system in Europe. Of the 162 patients with virus infections of the central nervous system, who were admitted between 1956 and 1958 to the Neunkirchen (Austria) Hospital, 89 (55%) had spring-meningoencephalitis. The onset of the disease is similar to that of poliomyelitis. Clinically, this virus infection can be divided into 3 forms: meningitis, meningoencephalitis, and paralytic meningoencephalitis. A particular characteristic of the latter form is the late

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appearance of paralysis which, despite a marked initial atrophy, has a tendency to complete regression. There is no specific treatment for spring-meningoencephalitis, any more than there is for poliomyelitis. In general, the course of the disease is mild. Among the 89 patients with spring-meningoencephalitis reported, only 5 (5.6%) died.

It is difficult to differentiate spring-meningoencephalitis due to virus infection from poliomyelitis by the anatomicopathological aspects of the central nervous system alone. The etiology of the disease can only be diagnosed correctly by means of serologic and virologic examinations. The importance of systematic laboratory investigations in all diseases of the central nervous system caused by virus infection is emphasized.

Polyarteritis Nodosa and the Nervous System. K. Koppang. Tidsskr. norske laegefor. **79**:679-683 (June 1) 1959 (In Norwegian) [Oslo].

Polyarteritis nodosa occurs more frequently than was previously believed. The nervous system is affected in about half of the cases. The predominating neurological symptom is polyneuritis, often with asymmetrical involvement. Symptoms from the central nervous system are less frequent. The possibility of polyarteritis nodosa should be considered in polyneuritis accompanied by fever, increased sedimentation reaction, and simultaneous symptoms from other organs. Positive biopsy findings are not necessary to establish the diagnosis in life. If polyarteritis nodosa is suspected, careful search for possible allergens, especially medicaments, is called for. The course of the disease can to some extent be influenced by cortisone treatment.

GYNECOLOGY & OBSTETRICS

A Study of the Aetiological Factors in Carcinoma of the Cervix Uteri in Guntur. P. S. Rao, R. S. Reddy and D. J. Reddy. J. Indian M. A. **32**:463-470 (June 16) 1959 [Calcutta].

The authors report on 758 patients with symptoms pointing to lesions of the uterine cervix, who were screened at the gynecologic outpatient clinic of the General Hospital in Guntur, India, between December, 1957, and February, 1959. To evaluate the relative incidence of carcinoma of the uterine cervix among different religious groups, patients of the same age-group attending the same hospital during the same period for diseases other than carcinoma of the cervix were grouped according to religion and served as contratest patients. All cases of carcinoma of the cervix were histologically confirmed except 30 cases.

Findings suggest that there is a definite relationship between the incidence of carcinoma of the cervix and the different religious groups. A high incidence of carcinoma of the cervix was observed among the Hindus and Christians whose partners were uncircumcised. The male partners of these patients showed higher grades of smegma accumulation. Carcinoma of the cervix was significantly low among the Moslems. No case of carcinoma of the penis was encountered among Moslem patients during the period of investigation. This emphasizes the causal role of smegma in carcinoma of the cervix. The peak incidence of carcinoma of the cervix was observed in patients between 31 and 50 years of age and in those who were in the premenopausal stage of life. The majority of the patients with carcinoma of the cervix belonged to the lower income groups.

Twenty out of 475 biopsy specimens obtained from patients with carcinoma of the cervix showed a definite association between chronic cervicitis and carcinoma of the cervix. Transition between cervicitis and neoplastic change could be demonstrated in every one of these 20 cases. It is pointed out that the recent experimental production of carcinoma of the cervix in mice by horse and human smegma should be evidence enough to frighten Americans to resort to mass circumcision of newborn male infants.

The Influence of Certain Etiological Factors in the Appearance of Cancer of the Cervix Uteri and of the Breast. C. Gros, R. Keiling and R. Renaud. Semaine hôp. Paris **35**:1968-1973 (June 12) 1959 (In French) [Paris].

At the Anticancer Center and Faculty of Medicine of the University of Strasbourg the authors studied the influence of race, marital status, and pregnancy on the frequency of cancer of the cervix uteri and of the breast. Out of 512 cancers of the cervix, 4 were in Jewesses, and among 724 cancers of the breast, 34 were in Jewesses. Cancer of the breast appeared significantly more frequently in Jewesses than in non-Jewesses, and cancer of the cervix appeared much less frequently in Jewish than in non-Jewish women. An attempt is made to explain the latter fact through hygienic conditions which would account for the presence of less preputial smegma, a substance which was demonstrated by Plaut and Khon Speyer to be cancerogenic. An ethnic explanation is that the Jews have a marked degree of consanguinity, and a genetic factor may be responsible for resistance of the cervix uteri to cancerogenic substances.

Marital status appears to play an important role in the relative frequency of these 2 cancers. Both cancer of the cervix uteri and cancer of the breast appear more frequently in married than in unmarried women, but this difference between the married and the unmarried is less marked in cases of cancer of the breast. The authors' percentages tally absolutely with those given by other investi-

gators in different countries. In attempting to define the influence of pregnancy, the authors found that there was a higher proportion of sterile married women with epithelioma of the breast than with epithelioma of the cervix. The frequency of cervical cancer increases rapidly with the number of pregnancies. Cancer of the cervix uteri is less frequent than cancer of the breast in women with 1 or 2 pregnancies, but it surpasses the frequency of cancer of the breast when there have been more than 2 pregnancies. The authors' statistics are in complete agreement with those of other cancerologists on this point. Lastly, they cite the fact that study by other investigators of the menstrual cycle, of the age at marriage and first pregnancy, and of the number of pregnancies shows much genitohormonal activity in women afflicted with cancer of the cervix uteri. The question is raised as to whether estrogens play a large part in the appearance of this cancer.

Effects of 17α-Methyl-19-Nortestosterone in Pregnancy and in Threatened Abortion. A. Foix, R. O. Bruno and J. Carpinacci. Obst. y ginec. latino-am. 17:229-235 (March-April) 1959 (In Spanish) [Buenos Aires].

The synthetic nor-steroid, 17α-methyl-19-nortestosterone (or methyl-estrenolone), has a marked progestational action with only a mild androgenic effect. It has, therefore, a wide field of application in gynecology. The authors studied its effects in 2 groups of patients. The first group was composed of 10 pregnant women, between the ages of 22 and 38 years, with pregnancies of 40 to 60 days, who had had spontaneous abortions or had become pregnant after treatment for sterility. Six had had at least one abortion; one had had 3 abortions. As a criterion for the administration and dosage of 17α-methyl-19-nortestosterone, special attention was given to the changes in the vaginal cytology. The treatment was started as soon as the index of acidophilic karyopyknic cells exceeded 20%. The initial dose was 2 to 5 mg. daily. Four days later the cytological test was repeated, and the dose was maintained, increased, or decreased according to the findings. This procedure was followed as long as the cytological conditions indicated the need for medication. In 6 patients the pregnancy was following a normal course when this article was written; 2 patients had normal deliveries at term; one had an abortion (probably due to torsion of the umbilical cord); and in one the treatment had to be discontinued because of intolerance symptoms, although the vaginal cytology had improved during the period of medication tolerance.

The second group was composed of 21 patients, between the ages of 23 and 32 years, who showed symptoms of impending abortion. Eight patients had metrorrhagia, 2 had pain, and 2 had both metrorrhagia and pain. Fifteen patients had had one or more spontaneous abortions. The pregnancy stage varied from 1 to 5 months. The doses of 17α-methyl-19-nortestosterone administered to these patients were higher than those administered to the patients in the first group. In some cases they reached 15 mg. daily until the symptoms of impending abortion had abated or disappeared. The treatment was then continued with smaller doses until normalization of the vaginal cytology was achieved. In 10 patients the pregnancy was following a normal course when this article was written; one had a normal delivery at term; 8 had abortions; and in 2 cases the results were unknown. Taking both groups as a whole, one-third of the patients had edema of the face and other signs of intolerance to the drug. The authors believe that the likelihood and severity of intolerance will be greatly reduced by administering 17α-methyl-19-nortestosterone by the sublingual route instead of the alimentary route used in this study. The results are termed encouraging, especially when one considers that all the patients studied had a manifest tendency to interruption of the pregnancy.

PEDIATRICS

Association of Type 2 Hemadsorption (Parainfluenza 1) Virus and Asian Influenza A Virus with Infectious Croup. A. J. Vargosko, R. M. Chanock, R. J. Huebner and others. New England J. Med. 261:1-9 (July 2) 1959 [Boston].

In the fall of 1957 a study to isolate new viruses and to associate these agents with clinical illness, including croup, was initiated by the virus section, Research Foundation of the Children's Hospital of the District of Columbia, and the laboratory of infectious diseases, National Institutes of Health. The 47 patients who are the subjects of this report were admitted to the Children's Hospital of the District of Columbia because of an acute croup syndrome during the year from October, 1957, through September, 1958. Specimens were collected during the same interval from 949 infants and children who were free of respiratory-tract illness. Those included hospital patients during the entire study period and children from the "well-child" and outpatient clinics. The mean age for the patients with croup was 24.7 months; that for the patients without respiratory disease was 24.6 months. Oropharyngeal swab specimens and serums taken from the latter patients were treated in the same manner as those from patients showing clinical respiratory illness.

Viral agents were recovered from 16 (or 34%) of the patients with croup. Hemadsorption virus type 2, which was recovered from 12 (or 25%) of the patients with croup, was the agent most frequently encountered. Hemadsorption virus type 1, croup-

associated virus, adenovirus type 1, and adenovirus type 5 were each isolated once. The association of hemadsorption virus type 2 with croup appears to be significant. The recovery of this agent from infants and children without respiratory-tract illness occurred at a rate of only 0.2%.

From the serologic data obtained in this study, a diagnosis of viral infection could be assigned to 71% of the children with croup. The viruses associated included influenza virus, hemadsorption virus types 1 and 2, croup-associated virus, and adenovirus types 1 and 5. The agents whose association with croup was best substantiated were hemadsorption virus type 2 and the virus of Asian influenza type A, both myxoviruses. The Asian influenza virus was associated with 5 (36%) of 14 croup illnesses during the month when that agent was most prevalent, and in 19% throughout the year. Infection with type 2 hemadsorption virus was associated with 17 (36%) of 47 patients with croup seen throughout the year. Evidence for infection with Asian influenza virus or hemadsorption virus type 2 was found in approximately 55% of all the croup patients studied. Infection with type 2 hemadsorption virus was found predominantly in boys, but its clinical features were not distinctive. In an addendum it is stated that the high level of association of hemadsorption virus type 2 with the croup syndrome described in this paper was maintained from October, 1958, through May, 1959. Hemadsorption virus type 2 was recovered from 7 (16%) of the 44 patients studied during this interval. Additional evidence for the role of hemadsorption virus type 1 in the croup syndrome was the isolation of this agent from 3 of the 44 patients.

The association of Asian influenza with croup is not surprising to clinicians, who have believed for years that influenza viruses may cause croup. The association of hemadsorption virus type 2 with croup is the most striking finding in the studies on hemadsorption viruses. These agents are new myxoviruses that will shortly be classified as Myxovirus parainfluenzae 3 (hemadsorption virus type 1) and Myxovirus parainfluenzae 1 (hemadsorption virus type 2).

Tuberculous Lesions in Children Who Have Been Inoculated with the BCG Vaccine: Observations in 56 Children Seen at a Sanatorium. N. Ebers, Tuberkulosearzt **13**:397-399 (June) 1959 (In German) [Stuttgart, Germany].

A study of 56 children shows that a diagnosis of active tuberculosis is made much too often not only in children in general but in those who have been vaccinated. The 56 children studied had been inoculated with the BCG vaccine. They were admitted to the Elisabethenberg Sanatorium, in Germany, between 1948 and 1958 with a diagnosis of "active tuberculosis." Detailed examination of these children revealed an active process in only 13 cases, and only 5 of the cases were attributable to genuine failure of the BCG vaccine to confer protection. The number of BCG-inoculated children who subsequently developed active tuberculosis was an exceedingly small fraction of the total number of tuberculous children who were admitted to the sanatorium during the same period.

Neonatal Thyrotoxicosis. S. N. Javett, B. Senior and S. Heymann. Pediatrics **24**:65-73 (July) 1959 [Springfield, Ill.].

The authors report on 2 cases of neonatal thyrotoxic exophthalmic goiter in infants born of mothers with exophthalmos and inadequately controlled thyrotoxicosis. The mothers, who had received treatment before conception with radioiodine (I^{131}) and thyroidectomy, were at the time of delivery not only thyrotoxic but markedly exophthalmic. The infants were desperately ill at birth with a state resembling thyroid storm. Intravenous and oral administration of Lugol's solution proved lifesaving. Medication was required for 4 or 5 weeks, the patients remaining well thereafter. Appraisal of the pathogenesis of neonatal thyrotoxicosis favors the transplacental passage of a thyroid-stimulating agent, probably derived from the mother's pituitary. The thyroid status of neonates born of mothers taking medication for thyrotoxicosis reflects the interaction between the transmitted thyroid-stimulating agent and the particular drug being employed.

Ectasia of the Coronary Vessels in the Course of Periarteritis Nodosa in a Nursling Aged 2½ Months. R. Turpin, L. Becquet, R. Gorin and J. Cruveiller. Semaine hôp. Paris **35**:1779-1786 (May 24) 1959 (In French) [Paris].

Periarteritis nodosa is so rare in infants aged less than one year that only about 20 reports are to be found in the literature, and some of these are open to question. The present case, which occurred in an infant, aged 2½ months, was a striking example of the contrast between the commonplace clinical syndrome and the wide diffusion of the ectatic lesions of the arteries of medium and small caliber. The clinical manifestations consisted of acute febrile rhinopharyngitis followed by diarrhea, abdominal meteorism, moderate enlargement of the liver, polynucleosis with eosinophilia (10%), and minimal albuminuria. The child had apparently recovered when death suddenly occurred within a few seconds. Autopsy revealed ectasia of the coronary vessels with involvement of various renal, hepatic, splenic, duodenopancreatic, mesenteric, and appendicular arterioles. The cerebral and pulmonary arteries, on the other hand, were not af-

fected. The integrity of the electrocardiographic tracings contrasted strongly with the intensity of the coronary lesions.

No possible cause, and in particular no therapeutic sensitization, by vaccination or treatment with antibiotics or chemotherapy, could be found for the appearance of periarteritis nodosa in this infant. The histopathological lesions suggested a latent, subacute process, extending over a period of several weeks, if not months, and compensated for during much of the time. This, of course, brings up the problem of a possible intrauterine cause.

Treatment of Disseminated Infantile Histoplasmosis With Amphotericin B. J. Little, J. Bruce, H. Andrews and others. Pediatrics **24**:1-5 (July) 1959 [Springfield, Ill.].

The authors report on 3 infants, under the age of 1 year, and a child of 3 years, who were treated for disseminated histoplasmosis with amphotericin B (an antifungal agent derived from an unidentified Streptomyces species found in a South American soil sample). The patients were given amphotericin B intravenously in a daily dosage which varied between 0.25 and 1.0 mg. per kilogram of body weight. The calculated amount of the drug was dissolved in 5% dextrose in water, so that a concentration of 1 mg. of drug per 10 ml. of solution was not exceeded. The rate of infusion was adjusted, so that the dose was given over a 6-hour period. The continuation of medication for 4 to 8 weeks is recommended, but 2 of the patients responded well to shorter courses. Headache, nausea, and vomiting were early toxic manifestations of therapy. Elevations of the level of nonprotein nitrogen in the blood, without other evidence of renal disease, have been observed. Chills, fever, and an anaphylactoid-like reaction with peripheral cyanosis were observed in one infant after the first injection. The use of an antihistamine drug and epinephrine in oil apparently controlled the reaction, so that therapy could be continued. The medications were discontinued after the 12th day of treatment without return of the reactions.

A definite diagnosis of disseminated histoplasmosis is desirable before therapy is started because of the technical difficulties of treatment with amphotericin B. The authors recommend the Heiner agar-gel technique for histoplasmin precipitin reaction as a diagnostic tool. In this technique antigens are prepared from stock cultures of fungi and from cultures freshly isolated from patients, and undiluted serums of patients are used for antibody sources. This test is easy to perform and has greater sensitivity and specificity than other immunological tests. The response of the 4 children in this series to therapy was gratifying. All the patients are doing well, and there is no indication of relapse or exacerbation. The response seems to warrant further trial of amphotericin B in this frequently fatal disease of infancy.

Citric Acid and Rickets: Recent Views on the Calcium-Phosphorus Metabolism. R. Rossi and R. Cremoncini. Minerva pediat. **11**:606-615 (May 19) 1959 (In Italian) [Turin, Italy].

A combined preparation of citric acid–calcium–phosphorus was given to a group of 30 infants with rickets and to a control group of 10 healthy infants and children, aged up to 10 years. The control group received a daily dose of 2.2 or 4.4 Gm. of the compound for 10 days. The serum calcium value tended to increase in 8 of the 10 infants and children of the control group after they had received the preparation, but it became normalized 10 days after the administration of the last dose. Phosphatemia and the concentration of phosphorus in the serum either increased or decreased as a result of the therapy.

Of the 30 infants with rickets, who ranged in age from 4 to 15 months, 3 had a moderately severe variety and 27 a mild variety of the disease. Among the latter group, 10 had previously received treatment with prophylactic dosages of vitamin D, 9 had previously received treatment with therapeutic dosages of vitamin D, and 8 had not previously received any treatment with vitamin D. The treatment with the combined preparation of citric acid–calcium–phosphorus lasted 2 months and consisted of daily doses of 700 mg. to the infants under 6 months of age, of a double dose to the infants under one year, and of a triple dose to older ones. Two therapeutic doses of vitamin D were administered intramuscularly to 5 patients who had previously received only the prophylactic dose of vitamin D and to 4 infants who had not previously received vitamin D. This treatment produced marked improvement in patients with the mild variety of the disease; it induced increase of the serum calcium value in 17 patients and a normalization of the phosphatemia and of the concentration of phosphorus in the serum in most patients. The treatment produced a fair improvement in patients with the moderately severe variety of the disease.

Hormonotherapy with an Anterior Pituitary Preparation for Bronchial Asthma and Certain Infantile Allergic Skin Disorders. P. Perrotta. Minerva pediat. **11**:616-621 (May 19) 1959 (In Italian) [Turin, Italy].

Hormonotherapy with an anterior pituitary preparation was instituted in 40 children, under the age of 12 years, with bronchial asthma and in 93 children, aged between 2 and 8 years, with recurrent urticaria or atopic dermatitis. The allergic nature of the bronchial asthma was presumed in

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about two-thirds of the patients, and the endogenous nature in the one-third. The ancestors of the children with bronchial asthma of allergic origin had frequently had diseases of an allergic nature. The preparation from the anterior lobe of the pituitary was administered intramuscularly to the children with bronchial asthma every other day in trimester courses, with a month-long, drug-free interval in between, for a period of 1 or 2 years. At the beginning the doses were small and were gradually increased afterwards. The type of preparation administered was changed several times to prevent the formation of antihormones. No other symptomatic treatment was given. All the patients were cured of bronchial asthma, 31 (78%) of them after the first year and the remainder during the second year of treatment. Inspection of the patients 2 years after the remission of symptoms confirmed the definitive cure of bronchial asthma.

The second group consisted of 65 patients with recurrent urticaria and of 28 patients with atopic dermatitis. Small or medium-sized doses were administered intramuscularly every other day for 2 trimesters, with a drug-free month in between. The relief from symptoms was faster in these patients than in those with bronchial asthma, and there were no sequelae. The first symptom to subside was pruritus. The author believes that the hormonal action of the preparation not only afforded relief from urticaria and eczema but also had an antiallergic effect.

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THERAPEUTICS

Reappraisal of the Hypoglycemic Action of Acetylsalicylate. A. Hecht and M. G. Goldner. Metabolism 8:418-428 (July [Pt. 1]) 1959 [New York].

The effects of salicylates on carbohydrate metabolism have found new clinical interest in recent years, and both hyperglycemic and hypoglycemic reactions to salicylates have been described. The authors undertook a reevaluation of the hypoglycemic effects of the salicylates in view of the growing use of orally administered hypoglycemic agents. Large doses of acetylsalicylate (4.8 Gm. per day) were given to 13 nondiabetic and 12 diabetic patients for 1 to 3 weeks and were tolerated well. A moderate though significant hypoglycemic effect was obtained in most instances. The higher the initial blood sugar level, the more marked was this hypoglycemic effect, which was manifested on about the third day of medication and persisted throughout the treatment period. Salicylate administration had an insulin-sparing effect and appeared to enhance the action of tolbutamide. Oral and intravenous glucose tolerance tests were performed, and insulin and glucagon tolerances were measured. The test results suggest that acetylsalicylate does not alter gastrointestinal glucose absorption, renal excretion of glucose, or insulin sensitivity. Hepatic glycogenolysis does not appear to be affected, nor does the hypoglycemic action seem to be mediated through the adrenal cortex. Since other work indicates that the effect does not depend on the presence of functioning pancreatic tissue, the mechanism of action is obscure.

Effects of the New Xanthine Derivative, Ro 1-8239, on Respiration and Circulation in Obstructive Pulmonary Emphysema. F. Barrera, G. G. Regalado, J. C. Dominguez and others. Rev. cubana cardiol. 20:16-39 (Jan.-March) 1959 (In Spanish) [Havana].

The effectiveness of a new xanthine derivative (X-D), Ro 1-8239, was studied in a group of 12 patients suffering from chronic pulmonary obstructive emphysema with cardiovascular involvement (chronic cor pulmonale). In all these patients complete clinical and radiologic examination showed dyspnea, both at rest and during effort, bronchial symptoms, diaphragmatic flattening and hypomobility, and intercostal space dilatation. In 6 patients the emphysema was in an advanced stage; in the other 6 it was of a moderate degree. In all the patients complete spirometric studies, as well as determination of residual air volume and total pulmonary capacity, were performed at rest and 30 minutes after the intravenous administration of 0.1 Gm. of Ro 1-8239. Intracardiac catheterization was performed in 5 patients, with administration of 0.1 to 0.2 Gm. of the X-D into the pulmonary circulation. Three of these 5 patients received a dose of 0.25 to 0.50 Gm. of chloral hydrate as a premedication. All 5 patients were examined within 30 to 60 minutes after the administration of the X-D. Three normal subjects and 15 patients with pulmonary emphysema, treated with aminophylline and dihydroxytheophylline in doses equivalent to the doses of the X-D given to the experimental group, served as a control group regarding the spirometric, ventilation, and arterial blood values. Eight patients with simple mitral stenosis formed the control group in the study of pulmonary circulation by catheterization.

The effects of the X-D were evidenced mainly in the changes observed in pulmonary ventilation and arterial blood. There was a significant reduction in the air spaces and in the ratio of these spaces to the tidal air volume, with a consequent increase in the alveolar ventilation and in the arterial pH. There was also a statistically significant drop in the arterial oxygen content and arterial saturation, which the authors attribute to the changes produced in the ratio of ventilation to perfusion throughout the lungs and/or to increased flow through poorly or nonventilated areas. These results suggest that Ro 1-8239 acts mainly upon small vessels, both pulmonary and systemic.

Methimazole and Carbimazole in Hyperthyroidism: A Comparison by a Double Blind Technique. T. H. McGavack. Am. J. M. Sc. 238:1-12 (July) 1959 [Philadelphia].

In 1949 Stanley and Astwood called attention to the highly suppressive influence of certain imidazoles on the uptake of iodine by the human thyroid gland. They were particularly impressed with the usefulness of methimazole (1-methyl-2-mercaptoimidazole) in suppressing radioiodine (I^{131}) uptake and controlling the manifestations of thyrotoxicosis. More recently Lawson, Rimington, and Searle have suggested that the imidazole action could be prolonged by the substitution of a carbethoxy group for the hydrogen of the mercapto group on carbon atom 2 of methimazole. In clinical trial, this compound, carbimazole, has proved about as effective, weight for weight, as methimazole in the management of thyrotoxicosis. From clinical reports, which cover considerably more than 1,000 patients in the case of each drug, carbimazole seems to have produced fewer severe toxic reactions (granulocytopenic and urticarial-febrile reactions) than methimazole.

In view of the claims made for carbimazole, it was decided to have a single group of workers test the activity of each drug without knowing the identity of either, and to make such tests on a weight-for-weight basis. The 2 drugs, identified only by code numbers, have been administered to 123 patients in a series of 203 trials. Methimazole was given initially to 68 patients, and carbimazole initially to 55 patients. The 2 preparations appeared to be equally effective, on a weight-for-weight basis, in controlling the manifestations of hyperthyroidism. Eight toxic reactions were encountered during the administration of methimazole, and 6 with carbimazole. Two of these in association with the use of methimazole were urticarial-febrile reactions. All remaining reactions were manifested by one, or a combination, of the following features: pruritus, localized rashes, and transient edema. It is concluded that both methimazole and carbimazole are effective thyroid blocking agents of approximately equal activity. Methimazole may be more toxic than carbimazole, but a good many more cases should be studied before a hard-and-fast conclusion is drawn regarding this statement, as the differences in the present study are not statistically significant.

Kanamycin. S. M. Finegold. A. M. A. Arch. Int. Med. 104:15-28 (July) 1959 [Chicago].

Kanamycin is a new bactericidal antibiotic which has been shown to be highly effective when given parenterally in the treatment of a number of resistant staphylococcic and gram-negative bacillary infections. The author reviews the literature concerning the use of kanamycin in man and in experimental animals. Used orally, it exerts a profound effect on the normal aerobic intestinal flora, and it has been effective, or has shown promise, in the treatment of some intestinal infections and carrier states. Kanamycin has been adminstered by a variety of routes other than the oral and intramuscular with good results. It has also been used topically or as an irrigating fluid in superficial lesions and wounds and has been applied as an ointment or as a cream. There was no evidence of irritation or of allergic reactions, and the results were generally good.

Toxicity inherent in the drug can be avoided or minimized with careful management. The most important type of toxicity noted with parenteral kanamycin therapy was damage to the 8th nerve, involving both auditory and vestibular functions but chiefly the auditory. Permanent auditory damage may be avoided by stopping the treatment on the appearance of tinnitus. So far there has been little evidence of progression of damage for long periods after the drug has been withdrawn. Care should be exercised in the treatment of elderly patients, because they are more subject to nephrotoxicity and sometimes develop relatively high serum creatinine values. Suggestions as to dosage, precautions to be observed in administering kanamycin, and factors predisposing to toxicity are described in detail.

Statistical Study of the Treatment of Acute Icterogenic Hepatitis with Deltahydrocortisone. P. Mainguet and J. Caroli. Semaine hôp. Paris 35:1974-1986 (June 12) 1959 (In French) [Paris].

The value of deltahydrocortisone (or prednisolone) in the treatment of acute icterogenic hepatitis was investigated by comparing the results obtained in 2 series of patients, one containing 90 patients treated with deltahydrocortisone and the other containing 60 patients treated with standard forms of therapy. The study showed that deltahydrocortisone was incomparably more effective than any of the older methods of treatment when given early in the course of the disease. Progression of the jaundice was checked, regardless of its intensity at the outset, if the patients were given deltahydrocortisone within the first week. No such result was obtained by any of the standard methods of treatment. The therapeutic effect of deltahydrocortisone was also favorable when it was given in the second or the third week of jaundice, but the results had less probative value because it could not be said that spontaneous clearing of the jaundice would have taken much longer.

Various authorities have questioned the value of corticotherapy, saying that the clearing of the jaundice and the improvement in the patient's

general condition are misleading and that the corticotherapy has no effect on the biological and anatomic disorders due to the hepatitis. These contentions are disproved by the results obtained in this study, which showed that deltahydrocortisone, when given early, not only cleared the jaundice and produced diuresis, but also led to the return of normal findings in the metabolic tests.

Corticotherapy is less effective and more dangerous when icterogenic hepatitis is prolonged or not promptly treated. Standard methods of therapy, particularly repeated duodenal intubations and cholecystostomy followed by transvesical drainage, retain their full value in such cases. The complications of corticotherapy must be kept in mind, and certain elementary precautions should always be taken. These include routine radiographic studies for the detection of gastric or duodenal ulcer (in suspicious cases) and of pulmonary tuberculosis, so that the corticotherapy can be supplemented, if necessary, by antiulcerous or antituberculous therapy. Similarly, the blood coagulation should be watched and anticoagulants given at the first sign of hypercoagulability. Finally, the arterial pressure and the urinary sugar level should be regularly checked. These precautions should prevent the occurrence of complications. Those few that may occur in spite of them are not to be compared with the benefits to be derived from the early use of deltahydrocortisone, which is the only method now available by which the development of icterogenic hepatitis can be halted at the start.

Iproniazid Hepatitis: Report of Five Cases and Review of Pertinent Literature. A. Felix, E. Schwartz and H. Rifkin. A. M. A. Arch. Int. Med. **104**:72-82 (July) 1959 [Chicago].

The authors review the literature concerning liver damage in patients treated with iproniazid, and present a report on the occurrence of hepatocellular jaundice in the course of iproniazid treatment in 4 patients. A 5th patient is also reported, who had no jaundice but in whom widespread focal necrosis of the liver was found at autopsy, which was attributable to iproniazid therapy. Jaundice has occurred in patients receiving a wide range of dose levels. Whether the total cumulative dose given or the daily dosage is significant in determining the onset of jaundice is not clear. Evidence of liver-cell injury and jaundice usually occurs only after 2 weeks of iproniazid treatment, and generally is delayed for several weeks. The degree of liver damage may vary from mild, transient alterations of liver function tests to overt jaundice and potentially fatal, widespread hepatic necrosis and hepatic coma. There is no specific treatment other than the recognized regimens for severe hepatic damage, including steroid therapy.

The pathogenesis of liver damage due to iproniazid is still unknown. Similarly, the relation of hepatitis due to iproniazid to that caused by a virus is not clearly understood. The possibility of a direct chemical hepatotoxicity, however, cannot be disregarded. The action of iproniazid as a potent inhibitor of amine oxidase, its chemical relation to hydrazine, and its possible involvement in the metabolism of pyridoxine suggest several ways in which it may exert a toxic effect on the liver. The effects of increased circulating amines, the possibility of heretofore unrecognized inhibition of other enzyme systems, and the possibility of interference in the metabolism of vitamin B complex, all require consideration as possible pathogenic factors in the production of liver damage by iproniazid. In view of recent clinical experience, iproniazid should undoubtedly be considered a potential hepatotoxic agent. Appropriate precautions in its clinical use should be taken. It is best to withhold the drug from patients with liver disease until the effects of iproniazid therapy in such patients have been adequately studied.

Oral Treatment of Diabetes Mellitus with 1-Cyclohexyl-2-*p*-Tolylsulfanylurea: The Behavior of Serum Cholesterol During the Course of Treatment. B. D'Alessandro, A. Brancaccio, R. De Luca and G. Jacono. Minerva med. **50**:1422-1426 (May 12) 1959 (In Italian) [Turin, Italy].

The authors studied the effect of Diaborale (1-cyclohexyl-2-*p*-tolylsulfanylurea), a new Italian preparation with hypoglycemic effect administered orally, on the serum cholesterol of 16 diabetic patients divided into 2 groups. The first group was composed of 11 patients with mild or moderate diabetes, who had not been treated with insulin before they were given oral treatment with Diaborale. The second group was composed of 5 patients who had been treated with insulin for a prolonged period. The values of cholesterolemia, though high in both groups, did not reach levels higher than normal. An almost total normalization of the values of glycemia was obtained during treatment with Diaborale in the patients of the first group. In these patients a slight decline in total cholesterol level, noticed early in the course of the treatment, was followed later by an increase which at times reached values higher than those noticed at the beginning of the treatment. No changes in total cholesterol level were observed during the treatment in a patient who had presented subnormal total cholesterol values in the beginning. The values of total cholesterol became normal in another patient who also presented subnormal values in the beginning. Ester cholesterol followed the same pattern as that of total cholesterol in 3 patients; the increase in the values of ester cholesterol in these patients occurred at the expense of

the free cholesterol which decreased. The increase in the values of total cholesterol coincided with an increase of the values of free cholesterol in 6 patients.

The values of cholesterol increased after withdrawal of insulin in 2 patients of the second group; during treatment with Diaborale, however, these values declined and were lower at times than the values observed at the beginning of the treatment. In one of these 2 patients glycemia responded to treatment with Diaborale and became normal; the values of ester cholesterol decreased, and those of free cholesterol increased slightly. Diaborale had no effect on the values of glycemia in the other patient; the level of total cholesterol remained unchanged; the level of ester cholesterol increased; and the level of free cholesterol declined.

A decline in the values of total cholesterol was observed in 3 patients of the second group who had discontinued taking insulin for some time or were taking it only at intervals; during the course of the treatment with Diaborale these values increased to a level higher than that present at the beginning in one of these patients. A decline in total cholesterol level was observed in the other 2 patients in whom Diaborale had no effect on the values of glycemia. Free and ester cholesterol values followed the same pattern as total cholesterol, except in one patient in whom an increase in the value of free cholesterol was observed. The authors believe that prolonged treatment with hypoglycemic drugs may result in a slow accumulation of the drug in the tissues and may cause some functional alterations, which are probably reversible, in the alpha cells of the pancreas.

PATHOLOGY

Laboratory Investigations on Occurrence of Pathogenic Staphylococci in Hospital Milieu. T. M. Vogelsang. Tidsskr. norske lægefor. **79**:517-523 (May 1) 1959 (In Norwegian) [Oslo].

Hospital infections due to pathogenic staphylococci have also increased in Norway. With the large number of antibiotic-resistant staphylococci which continue to occur in hospitals such epidemics can be expected to increase in frequency. When staphylococcus infections appear in a hospital department, cooperation between the division and the bacteriological laboratory should be established as quickly as possible. Specimens from all infectious foci and from nose and throat of personnel and patients should be submitted for laboratory examination. Supplementary examinations may be necessary. The isolated staphylococcus strains are typed. If the examination is made early in the epidemic, perhaps only one or two persons are carriers of the epidemic strain. If patients are carriers they must be properly isolated. If members of the personnel are carriers they should be granted leave for a time. Since many persons are intermittent carriers, there is thus a good chance that the epidemic strain can disappear from the upper respiratory tract during the stay away from the hospital.

How Reliable Is Biopsy of Rectal Polyps? A Clinical and Morphological Study of 107 Cases. C. A. Hellwig, and E. Barbosa. Cancer **12**:620-624 (May-June) 1959 [Philadelphia].

The authors aimed to determine how reliable biopsy of rectal polyps is in helping the surgeon decide between abdominoperineal resection and polypectomy, without minimizing the chances of a cancer cure. The gross and microscopic findings for all rectal polyps that had been examined in the laboratory of the pathology department, Hertzler Clinic and Hertzler Research Foundation, Halstead, Kan., from 1951 to 1957, were reviewed and coordinated with the clinical findings, including follow-up observation. One hundred forty-two polyps were removed from 107 patients. Eighty-seven adenomatous polyps were regarded as benign, 28 as malignant, and 12 as invasive carcinomas. In addition, 15 biopsy specimens were diagnosed as villous papillomas, 5 of them as cancerous. Most investigators agree on the importance of removing the whole polyp for careful histological examination. Particularly in pedunculated tumors, the necessity of having the whole pedicle available for microscopic study seems generally recognized.

The biopsy material available to the authors was far from ideal with regard to the completeness of the lesions. They more often received small bits of tissue than a polyp in its entirety. Seldom did they see a polyp with pedicle intact. Follow-up observations were successful in 90 of the 107 cases (84%). A second specimen was obtained from 37 patients, either as a second biopsy or by radical resection. The remaining patients had the polyps removed by electric snare and fulguration of the base. There was complete agreement between biopsy and final diagnosis in 79 of the 90 cases, partial agreement in 7 cases, and disagreement in 4 cases. The 90 patients on whom there was complete follow-up included 20 with noninvasive carcinoma who had polypectomy and in whom invasive carcinoma did not develop. The results of biopsies in villous papillomas were disappointing. In 3 instances, the biopsy specimen showed atypia or carcinoma in situ, while the examination of the resected specimen revealed carcinoma that had spread to the submucosa. A specimen from one adenomatous polyp was diagnosed as atypia, while a second biopsy and the final specimen showed a highly malignant invasive adenocarcinoma.

The authors emphasize that atypia, cancer in situ, and intramucosal focal carcinoma in rectal polyps should not be diognosed as adenocarcinoma. Except in cases in which a high grade of malignancy is present, a diagnosis of cancer is not justified when no invasion of the submucosa can be demonstrated. Biopsy diagnosis of villous papillomas is often unreliable, because focal areas of cancer may be present in the center of the lesion, while the peripheral portions are benign. In 4 of our 12 invasive carcinomas, the first biopsy revealed benign or atypical changes, while the second biopsy or the resected specimen showed invasive carcinoma. Small size, or the presence of a pedicle, is no guarantee that a given polyp is benign. Regardless of a clinically benign appearance, every polyp should have an adequate biopsy before it is destroyed by fulguration.

Lesions in Upper Portion of the Gastrointestinal Tract Associated With Intracranial Neoplasms. J. A. Spencer, C. G. Morlock and G. P. Sayre. Gastroenterology **37**:20-27 (July) 1959 [Baltimore].

At autopsies performed at the Mayo Clinic between 1946 and 1951, acute lesions of the upper part of the alimentary tract, such as petechiae, ecchymoses, ulcerative esophagitis, erosions, acute ulcers, and autolysis, were found in 148 (54%) of 274 unselected consecutive patients with intracranial neoplasms. These acute lesions of the upper part of the alimentary tract were found in only 173 (26%) of 666 patients with no significant intracranial lesions who served as controls. The incidence of coexistence of intracranial neoplasms and acute lesions in this part of the digestive tract thus has been much higher than could be expected to occur statistically by chance alone. The intracranial neoplasms in the 274 patients were interpreted as representative intracranial lesions, since in 255 (93%) complicating intracranial factors, such as infarcts, edema, hemorrhage, infection, demyelinizing disease, or surgical defects, were present. Extracranial factors which could have induced the lesions of the digestive tract were present in 82 (55%) of the 148 patients who had coexisting gastrointestinal lesions and intracranial neoplasms. These complications lend some doubt to the significance of the high incidence of coexistence of these lesions as observed in this study.

Type and location of the intracranial neoplasms could not be correlated with the acute lesions of the gastrointestinal tract. Acute changes of the upper part of the alimentary tract were found in only 50% of the patients in whom a gross pathological process involved the hypothalamus, and only 23% of the patients with acute lesions of the upper portion of the digestive tract had gross involvement of the diencephalon. Acute intracranial lesions other than increased intracranial pressure and cerebral edema were more frequently associated with acute gastrointestinal changes than were subacute or chronic intracranial lesions or the absence of lesions. Attempts to correlate clinical and pathological findings were unsuccessful. Except when gastrointestinal bleeding became evident, the presence of acute gastrointestinal complications of intracranial neoplasms could not be predicted clinically. Acute lesions of the digestive tract probably were a decisive factor in the death of 16 patients with intracranial neoplasms. Chronic and healed peptic ulcers were not found any more frequently in patients with intracranial disease than in those without intracranial disease and, therefore, should not be classified as "Cushing ulcers."

Intracranial Infections Causing Esophagomalacia and Gastromalacia: A Postmortem Study of Eleven Cases (V. Ulcer and Brain). J. B. Dalgaard. Gastroenterology **37**:28-34 (July) 1959 [Baltimore].

The author reports on 6 female and 5 male patients, between the ages of 2 months and 77 years, with cerebromeningeal infections who died and in whom acute peptic ulcers were found at autopsy performed at the University institutes of pathology in Aarhus, Denmark, and Bergen, Norway, between 1949 and 1956. These 11 cases were observed among 3,000 autopsies, including 60 cases of cerebromeningeal infections. Of the 11 patients, 2 had tuberculous meningitis, 3 had nonspecific meningitis, 2 had complicated cerebral abscesses, and 4 had encephalitis which was associated with toxoplasmosis in 1. Three patients were infants less than 1 year old, and 2 others were children, 7 and 8 years old. Of the 11 patients, 10 had the type of peptic lesion known as perforating esophagomalacia or gastromalacia. Infectious cerebral lesions seem especially prone to induce this type of peptic lesion. Such lesions are agonal but are always initiated during life; the actual perforation may occur before death (often being the ultimate cause of death) or it may occur after death. Intracranial infection is an uncommon but typical cause of neurogenic peptic ulceration.

The Preservation of Human Bone Marrow at −79 C. U. Torelli. Minerva med. **50**:1390-1392 (May 9) 1959 (In Italian) [Turin, Italy].

Human bone marrow remains viable for 4 or 5 days when stored at 4 C temperature and for about 2 weeks when kept in a culture. Viability can be maintained for a much longer period of time by suspending the bone marrow in a glycerol solution and freezing it at a −79 C temperature. The author describes an apparatus which he has prepared for storing human bone marrow at a low temperature. The apparatus, basically similar to that used by

Polge and Lovelock, consists of a Dewar flask of 4,500-ml. capacity. The cover of the flask is made of zinc and has a cylindrical container of 90-mm. diameter, also made of zinc, on its inner side. A smaller cylindrical container, made of copper, with a 300-ml. capacity, is placed inside the zinc container. A 100-watt resistor, through which passes a current whose intensity is regulated by a rheostat, occupies the space between the 2 cylindrical containers.

The Dewar flask is filled with a mixture of alcohol and dry ice; the space between the 2 cylindrical containers is filled with glycerol, and the internal container is filled with alcohol. The bone marrow mixed with an equal quantity of glycerol is put in vials, and these are submerged in the alcohol of the inner container. The current is turned on, and the cover is placed on the flask, so that the large zinc container is immersed in the alcohol. the temperature of which has been reduced by the dry ice to —79 C. The resistor prevents a sudden drop of temperature inside the smaller container. Freezing inside this container occurs at the rate of 1 C every 90 seconds from 0 C to —20 C and at the rate of 5 C per minute from —20 C to —60 C, after which the temperature falls rapidly to —79 C.

Normal temperature is restored to the contents of the vials by immersing them in a 37 C bath. The bone marrow separated from the glycerol is put into an empty Baxter flask, and 10 ml. of a 33% glucose solution is added for every 20 ml. of bone marrow; the contents are agitated for a few minutes, and later 30 ml. of Tyrode's solution is added for every 20 ml. of bone marrow. After a 2-minute rest an additional 120 ml. of Tyrode's solution is added, and the suspension is ready to be injected into the cubital vein. The author believes that this method of prolonged preservation will make human bone marrow available not only for homologous grafts but also for autogenous grafts.

Bilateral Cortical Necrosis of the Kidneys in the Course of Malignant Arterial Hypertension. J. C. Pimentel and R. do Rosário. Gaz. méd. port. **12**: 384-394 (Jan.-Feb.) 1959 (In Portuguese) [Lisbon].

Bilateral cortical necrosis of the kidneys is frequently found in women in association with pregnancy, but it may also occur in men and be associated with chemical intoxications or infectious diseases. The authors report on a case in which bilateral renal necrosis occurred in association with malignant arterial hypertension; they believe that this is the second case of this nature to appear in the medical literature. A 54-year-old man was admitted to the Gama Pinto Institute in Lisbon because of gradual loss of vision and mental confusion. He presented a history of arterial hypertension of a few years' duration and had lately been suffering from persistent headache, anorexia, dizziness, ear buzzing, and insomnia.

The diagnosis of malignant arterial hypertension was made, and the patient was treated with sedatives, intramuscularly administered papaverine, intravenously administered hypertonic dextrose solution, and parenteral feeding. His condition deteriorated in spite of the treatment. Anuria and coma occurred, and the patient died 5 days after admission to the hospital. At autospy the pathological findings revealed necrosis in all the structures of the renal cortex (glomeruli, tubes, vessels, and interstitial tissue) in association with the lesions that are typical of malignant arterial hypertension. The authors believe that the vascular lesions characteristic of malignant arterial hypertension may cause unilateral or bilateral renal necrosis, depending on whether or not the hypertensive condition has a renal origin.

Hormones and Carcinogenesis. O. Mühlbock. Nederl. tijdschr. geneesk. **103**:949-952 (May 2) 1959 (In Dutch) [Amsterdam].

The question whether hormones can exert a carcinogenic effect has been repeatedly investigated in recent years, and some published reports of such studies are cited by the author. A survey revealed that hormones presumed to be carcinogenic all have growth stimulating effects. Thyroid tumors have been produced experimentally by thyrotropic hormones; tumors of the adrenals, by the adrenocorticotropic hormone (ACTH); and various types of ovarian and testicular hormones, by gonadotropic hormones. It should be remembered, however, that the commercially produced hormones are derived from slaughtered animals, and, as a result, type specificity and antibody formation are involved in their action. In the female secondary sex organs, such as the breast and uterus, tumors have been produced by estrogenic hormones. Breast tumors have also been produced by the mammotropic hormone of the hypophysis. Hormones of the hypophysis with stimulating effects on organs such as the gonads, adrenals, or thyroid take first place among hormones with carcinogenic effects, and the steroid hormones are second in importance. Hormones such as insulin and thyroxin, which influence the metabolism in general but not a specific organ, have no carcinogenic effect. The somatotropic or growth hormone also has a systemic metabolic effect, but it has been possible to induce tumors in rats with pure growth hormone; the tumors thus produced ranged from sarcomas and adenocarcinomas to lymphoid tumors.

Whereas the connection between growth stimulation and carcinogenic effect is clear in endocrine organs and in secondary sex organs, it is doubtful

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in other organs and in lymphoid tissue. The action of estrogenic hormones as leukemia-inducing factors is still obscure, and likewise obscure is the mechanism by which skeletal and liver tumors develop under the influence of hormones. There is some evidence that the action of estrogenic hormones on the renal tubules of hamsters can be interpreted as a growth stimulus, which may be the first step in the development of renal tumors.

The carcinogenic effect of a hormone is largely dependent on the amount of hormone that acts on an organ. For instance, estrogenic hormone may induce breast cancers in castrated male mice; if the amount given is only equal to that physiologically present in female mice, relatively few breast tumors develop and at a rather advanced age; if, however, a dose 16 times as great is administered, breast tumors develop in all animals and at a younger age. The author's own studies, reported some years ago, revealed that the sensitivity of the organ to hormone effects also is important, in that with high sensitivity normal amounts of hormone may cause tumor formation. Furthermore, the author and a co-worker also observed a difference in the carcinogenic effect of a hormone, depending on whether the hormone was given continuously or interruptedly, the incidence of tumor development being much greater with continuous administration. Finally, the time of life during which hormones are given is important; thus, whereas hormone administration begun early in life produces breast tumor in a high percentage of patients, when the hormones are given during the second half of life, they exert a carcinogenic effect only occasionally. Hormone administration is usually given to middle-aged persons.

The Early Lesions of Aortic Atherosclerosis in Cali, Colombia. C. Restrepo and H. C. McGill Jr. A. M. A. Arch. Path. 67:618-623 (June) 1959 [Chicago].

This study represents one part of a continuing cooperative project between several pathology laboratories, which aims to write the natural history of atherosclerotic arterial lesions for different population groups in different geographic regions. Data of this same type derived from autopsy populations of New Orleans, Guatemala, and Costa Rica have been reported previously. The extension of this study to Colombia has been of particular interest in view of the fact that Colombia, according to vital statistics, has one of the lowest death rates from arteriosclerotic heart disease in the world.

The aortas of 289 persons, between 1 and 40 years of age, from a large charity hospital and a medicolegal service in Cali, Colombia, were quantitatively evaluated for the extent of the various types of atherosclerotic lesions. These figures were then compared with similar data for New Orleans Negroes, New Orleans whites, and Guatemalans. Fatty streaks were found to increase rapidly in extent during the second decade in Colombians, just as in other groups, and the hypothesis that this development of fatty streaks is related to the hormonal changes of puberty is supported. Despite having more fatty streaks in the third decade, the Colombians developed fewer fibrous plaques than the New Orleans whites, suggesting again that different factors control the progression of the different types of lesions. In view of the presumed relationship between lesions and clinical disease, these data on aortic lesions are not consistent with a low rate of arteriosclerotic heart disease such as is indicated by the vital statistics for Colombia.

RADIOLOGY

Radiologic Picture of the Lung in Marked Mitral Stenosis: Clinical, Hemodynamic, and Surgical Correlations. F. Galland, S. Aranda, S. Aceves and N. Dorbecker. Arch. Inst. cardiol. México 29:145-174 (March-April) 1959 (In Spanish) [México, D. F.]

The need for an accurate diagnosis of the degree of mitral stenosis, for the detection of association with other valvulopathies, and for an appraisal of the results of surgical correction has led to the present general interest in the radiologic study of the patient suffering from mitral stenosis. The authors studied 20 patients in whom mitral stenosis was either the only or the predominant pathological condition, and in whom the stenosed mitral area was smaller than 1 sq. cm. as determined by the surgeon at commissurotomy. Ten of these patients were men, and 10 were women, their ages ranging from 13 to 45 years. Besides the clinical and hemodynamic study of each patient, preoperative and postoperative teleradiograms were taken in each case, under the usual incidences (postero-anterior, right antero-oblique, and left antero-oblique). The postoperative radiograms were taken during the first 2 months after surgical intervention, then 2 to 6 months, 6 months to one year, and after one year following the operation. Clinically, the patients were classified into 4 groups according to the degree of pulmonary capillary hypertension, of dyspnea, and of size of the mitral area involved.

The preoperative picture of the lung showed hilar nebulosity in all the patients, laminar effusion in 14, horizontal scissure with abnormal characteristics in 9, lightly spotted areas in 15 and heavily spotted areas in 4 (the latter resembling the radiologic aspects present in hemosiderosis), and septal lymphatic lines (lines B of Kerley) in 17. A comparison of the clinical and radiologic pictures showed that the preoperative picture of the lung was correlated with the capillary pres-

sure in 9 (64.2%) of the 14 patients in whom catheterization had been performed; with the clinical symptoms of venous capillary hypertension in 16 (80%) out of 20 patients; and with the size of the mitral area in 18 (94.7%) out of 19 patients. During the postoperative stage, as the patient improved and the degree of dyspnea decreased, the radiologic picture of the lung approached the normal image, showing a correlation between the clinical and the radiologic pictures in 16 (88.8%) out of 18 patients in relation to venous capillary hypertension and in 17 (94.4%) out of 18 patients in relation to the degree of mitral opening obtained. The authors conclude that, as a rule, there exists in patients with mitral stenosis a correlation between the radiologic picture of the lung, on the one hand, and the venous capillary hypertension and the involvement of the mitral area, on the other, and that the changes in the postoperative radiologic picture may serve, on the whole, as means of evaluating the effectiveness of the operation.

The Roentgenologic Evaluation of Systemic Lupus Erythematosus. T. L. Taylor and H. Ostrum. Am. J. Roentgenol. 82:95-107 (July) 1959 [Springfield, Ill.].

The authors report on findings in the roentgenograms obtained at the Philadelphia General Hospital from 23 patients with proved systemic lupus erythematosus. These findings depended on the stage of the disease during which the roentgenograms were taken, and they reflected acute or chronic inflammatory changes in the pleura, lungs, and pericardium. In the initial acute stage, these changes consisted of bilateral moderate or massive pleural effusion, massive pericardial effusion, subpleural inflammation, perivascular inflammation, small areas of interstitial pneumonitis at the lung bases, and small areas of segmental pneumonitis at the lung bases. In the resolving stage, the findings included those of minimal unilateral or bilateral pleural effusion, minimal to moderate pericardial effusion with straightening of the left border of the cardiac shadow but without widening of the heart base, small linear areas of "plate-like" atelectasis at the lung bases, and areas of segmental atelectasis at the lung bases. In the chronic stage, the chest roentgenograms showed that, unless the nephrotic syndrome was present, the cardiac outline returned to normal or cor pulmonale developed. In some patients the outline of the pulmonary conus remained particularly obscured by fibrosis which filled in the pericardial spaces around the conus. The pleural effusion may completely disappear. Fine pulmonary scars may be seen at the lung bases, frequently associated with "tenting" of the pleura, or the lungs may appear clear. Multiple pulmonary infections occurred. During period of exacerbation, pleural and pericardial effusions were limited by adhesions; fine linear densities were intermingled with small areas of interstitial pneumonia at the lung bases; basal areas of segmental pneumonitis occurred; subpleural and perivascular inflammation was present.

A history of joint pain and the pericardial, perivascular, interstitial, and pleural inflammatory changes which are visible in chest roentgenograms provide evidence which is almost pathognomonic of acute systemic lupus erythematosus. Delayed renal function may be evident on intravenous pyelography. The relationship between systemic lupus erythematosus and destructive joint changes typical of rheumatoid arthritis is unproved. In the patients of this series, there were no instances of demonstrable joint changes other than soft tissue edema and those changes attributable to Raynaud's syndrome.

Pulmonary Alveolar Proteinosis: Report of Two Cases. G. F. Lull Jr., J. C. Beyer, J. G. Maier and D. F. Morss. Am. J. Roentgenol. 82:76-83 (July) 1959 [Springfield, Ill.].

The authors report on a 23-year-old man and on a 40-year-old woman with pulmonary alveolar proteinosis, a disease which was first described by Rosen in 1958, and 28 cases of which were collected from the literature. The name of the disease is a misnomer in that the intra-alveolar substance is not a protein, but until the substance is accurately identified, the name will remain. The causation of the condition is unknown. Whether it is a truly new disease has not been established, but it appears not to have been present before 1953, and it has been recognized with increasing frequency since then. The changes revealed by the chest roentgenograms of the 2 patients were strikingly similar to those reported by other workers. The characteristic appearance has been that of a fine granular or feathery type of parenchymal density, soft in appearance and usually widely disseminated. Its radial distribution from the lung hili resembled severe pulmonary edema in the collected cases, while in the authors' patients this radial distribution was not especially apparent, and the densities tended to be increased in number and to be more confluent toward the lung bases.

Both patients were subjected to thoracotomy for lung biopsy. A single wedge of tissue was removed from the right middle lobe of the man and wedges were removed from the apical posterior segment of the upper lobe and from the lingula in the woman. In both patients, there were patchy, confluent areas of a granulomatous-like process without evidence of discrete nodules or of caseation, and with interspersed areas of grossly normal lung parenchyma. Microscopically, there was a patchy, alveolar filling

process with the material consisting of a granular acidophilic substance which was PAS-positive. The interalveolar septums were not involved per se, but proliferation of large cells, somewhat like lipophages, was noted from the alveolar walls. These were interpreted as septal cells, and granules within their cytoplasm were also PAS-positive. While histopathological diagnosis is required to confirm the diagnosis, pulmonary alveolar proteinosis may be suspected in a patient who shows extensive pulmonary changes on the chest roentgenogram in the presence of essentially normal findings on physical examination of the chest. Inasmuch as pulmonary alveolar proteinosis is being seen with increasing frequency, since it is a chronic disease, and inasmuch as there appears to be a high mortality rate, with deaths resulting from superimposed infection or from obliteration of the respiratory surface, the search for the causative agent and for adequate therapeutic measures must be pressed with vigor.

Idiopathic Unilateral Hyperlucent Lung: A Roentgenologic Syndrome. H. N. Margolin, L. S. Rosenberg, B. Felson and G. Baum. Am. J. Roentgenol. 82:63-75 (July) 1959 [Springfield, Ill.].

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The authors report on 4 male patients, aged 12, 25, 28, and 40 years, respectively, with abnormal radiolucency of an entire lung or lobe which could not be classified among the usual entities known to cause this appearance. In addition to the abnormal translucency mentioned, the chief roentgen-ray features included normal or small size of the affected lung or lobe; maintenance of almost constant volume of the affected portion of the lung during changes in respiration; a small hilar shadow with sparseness of the intrapulmonary vascular markings; and an unusual bronchiectatic pattern without evidence of obstruction of the larger bronchi. This combination of the roentgen-ray signs of unilateral emphysema, a normal main bronchus (supplying the affected portion of the lung) but abnormal small bronchi, and a diminished intrapulmonary vascular pattern resulted in a readily recognizable complex, which appears to represent a genuine roentgenologic entity, for which the term "idiopathic unilateral hyperlucent lung" is suggested. Not enough is known of its pathogenesis to justify a more specific title.

The clinical and laboratory aspects of the condition indicated that it is associated with a disability of varying degree, perhaps related to impairment of pulmonary function. Differentiation of this syndrome from other conditions causing abnormal unilateral radiolucency can be made, bronchography being of particular value in this regard. The question of separating unilateral hyperlucent lung from the entity of hypoplasia of a pulmonary artery deserves particular consideration, since the diagnosis of hypoplasia of a pulmonary artery is very difficult. Although all 4 patients appeared to show unilateral deficiency in pulmonary arterial circulation, it is believed that hypoplasia of a pulmonary artery is probably a separate entity from idiopathic unilateral hyperlucent lung, but an absolute differentiation between them may not be possible until there is further knowledge of the pathogenesis and causation of these conditions.

Blood Counts in Relation to African X-Ray Staff. E. F. Allen, A. Cruickshank and L. R. Whittaker. East African M. J. 36:274-275 (May) 1959 [Nairobi, Kenya].

Total and differential white blood cell counts were routinely made on staff exposed to ionizing radiations in the x-ray department of the King George VI Hospital, Nairobi, Kenya. It was found that, in comparison with accepted European constants, the blood counts of the European staff were within normal limits, while in the African staff relative leukopenia and lymphocytosis were common. Leukopenia and a relative lymphocytosis can suggest an early blood change due to ionizing radiations; however, by direct monitoring it was found that none of these members of the staff received exposure greater than 0.025 rad per week. Therefore, as a baseline for future analysis of the leukocyte counts of the African staff of the x-ray department, the total and differential leukocyte counts of 80 students from the Medical Training Center in Nairobi were determined. The results obtained demonstrated that, in assessing a possible radiation hazard, the standard accepted as normal for the European staff cannot be applied to the African staff. The standard quoted in this paper is applicable to Nairobi (altitude, 5,000 ft.) and will not necessarily apply in other areas. Radiation monitoring by the film method is the most accurate method available and should be regularly observed on staff exposed to ionizing radiations. Nevertheless, quarterly routine total and differential blood counts should be taken in order to ascertain that there is no individual susceptibility to ionizing radiation.

PUBLIC HEALTH

The Case Against B. C. G. A. S. Anderson, L. B. Dickey, M. L. Durfee and others. Brit. M. J. 1:1423-1430 (June 6) 1959 [London].

Tuberculosis differs from smallpox in that an attack does not result in dependable immunity. Thus there is slim premise for attempting to produce immunity artificially. Allergy to tuberculo-

protein is not an indication of immunity, but is a prerequisite to the development of clinical tuberculosis. The human body defends itself better against first invasions with tubercle bacilli than it does against reinfections. Clinical disease develops only in persons who have been previously sensitized to tuberculoprotein. Accurate differentiation between primary pulmonary infiltrates and clinical lesions of reinfection type is of the utmost importance. Without this, erroneous deductions are made with reference to efficacy of BCG vaccine. For example, it may be credited with beneficial effects when primary infiltrates are grouped with lesions of reinfection type, so it appears that clinical disease develops in more control persons than in those in whom primary lesions have been produced in the skin by BCG vaccine. An adequately controlled study of BCG vaccination among people living in their homes has never been accomplished. It has been found impossible. However, well-controlled studies were conducted among the cattle herds in the United States and Canada and elsewhere. BCG vaccine failed and was abandoned. In the few places in which it is still used with major dependence on it, tuberculosis remains a serious problem among cattle.

Among human beings the most phenomenal accomplishments in eradication of tuberculosis have been achieved in countries in which little or no BCG vaccine has been used, including Iceland, Hawaii, and the Netherlands. In countries in which BCG vaccine has been employed extensively, including Denmark, Norway, and Sweden, marvelous results have been achieved, but along with BCG vaccine there have been employed the same fundamental methods which alone brought about the greatest accomplishments in history. This also applies to special groups such as students of nursing and medicine. The numerous values of the tuberculin test in diagnosis and epidemiology are lost to persons whose tissues have been sensitized to tuberculoprotein by BCG vaccine. Bacteriological investigations have revealed that cultures designated BCG were not composed of just a single bacterial form such as Calmette and Guérin produced, but of multiple bacterial forms, which differed in many of their properties, and some of which were definitely invasive for animal tissues. No two cultures were alike. Evidently different mutants and changes had occurred in each of the cultures studied. Apparently mutants produced destructive disease in animals on deficient diet, those which were silicotic, and in at least two species of normal animals. In human beings, they sometimes caused lesions at the site of administration and of regional lymph nodes, as well as other organs, and death in at least a few cases. Calmette repeatedly warned that no living organism capable of producing tubercles in animal tissues should be administered to human beings. If methods of preventing mutations in cultures have been or can be devised, there is no assurance that it will not occur after the living organisms are introduced into human tissues.

The 17 American workers who wrote this review believe that inasmuch as most BCG proponents recommend it only for those uninfected, it would not be applicable to the about 56 million citizens in the United States who already are tuberculin reactors. Moreover, among the remainder the tuberculous infection attack rate has reached such a low ebb that relatively few would be expected to become infected. Furthermore, treatment now available is effective for recently developed clinical lesions.

Long-term Effectiveness of B. C. G. Vaccination of Infants in Close Contact with Infectious Tuberculosis. J. Lorber and P. C. Menneer. Brit. M. J. 1:1430-1433 (June 6) 1959 [London].

The authors report on 267 children who were aged less than 2 years when they were vaccinated with BCG vaccine between 1949 and 1952. Of the 267 children, 261 were followed up 5 or more years after their vaccination. Of these, 10 (3.7%) were alive and well, but their parents refused reexamination. Three (1.1%) had died of other causes than tuberculosis. The remaining 248 (92.9%) were reexamined and tuberculin-tested, and chest roentgenograms were obtained from 235. There were no deaths from tuberculosis. Only 2 had minor clinical symptoms associated with tuberculous lung lesions which healed by calcification, and one additional child had a calcified lung lesion. Only 4 of the 248 children on whom tuberculin tests were performed had reverted and were tuberculin negative. The 4 negative reactors were revaccinated and they responded with a typical primary BCG lesion like tuberculin-negative children.

All of the vaccinated children were household contacts of tuberculous persons including parents, grandparents, and other persons. In contrast to the children, 39 (15.7%) of these tuberculous persons died of their tuberculosis and 28 (11.3%) still had active disease at the time of the follow-up. As there were no comparable controls it cannot be shown conclusively that BCG vaccination prevented tuberculosis in this group of children. Nevertheless, the results obtained are highly suggestive that this was the case. The facts that from such a particularly unfavorably situated group of infants none died of tuberculosis and that symptoms which could possibly be attributed to tuberculous infection developed in only 2 suggest that the vaccinations were of value. The prolonged effectiveness of the vaccination, as judged by the persistence of the positive tuberculin reaction in 98% of the children retested, is emphasized.

BOOK REVIEWS

Nutrition and Atherosclerosis. By Louis N. Katz, M.D., Director, Cardiovascular Department, Medical Research Institute, Michael Reese Hospital, Chicago, Jeremiah Stamler, M.D., Director, Heart Disease Control Program, Chicago Board of Health, and Ruth Pick, M.D., Assistant Director, Cardiovascular Department, Medical Research Institute, Michael Reese Hospital. Cloth. $5. Pp. 146, with 67 illustrations. Lea & Febiger, Washington Sq., Philadelphia 6, 1958.

This is the second monograph concerned with atherosclerosis from the Medical Research Institute of Michael Reese Hospital. Like the first, its value rests especially in the list of references—a nearly complete register of the scientific literature dealing with atherogenesis to the middle of 1958; the earlier monograph had carried them as far as 1953. Beyond this catalogue of references the monograph has some serious limitations. The authors tend to be preoccupied with their own publications. This is understandable, but when, as often happens, the authors cite one of their own reviews as a source which is as readily available in its original form I think they do an unscholarly thing. Most scientists will not need these authors for interpreters.

The authors begin with a statement of a theory that is, frankly, a corker. It is, in the first place, a monumental problem for grammarians—"the nutritional-metabolic cholesterol-lipid-lipoprotein theory of atherogenesis." This seems to take care of almost any eventuality. To say that atherogenesis is influenced by nutritional and metabolic factors is surely conservative, one might even say trite. The authors say, in describing this theory, "The atherogenic alterations . . . are by-products of an habitually unbalanced diet excessive in total calories, empty calories, total fats, saturated fats, cholesterol, refined carbohydrates, salt and inadequate (relatively and/or absolutely) in certain essential nutrients (vitamins, minerals, essential amino acids and essential fatty acids) and in bulk." The fact that these authors can find nothing good about the finest diet in human history is perhaps the tip-off to their limitations in preparing such a book. They are not familiar with the science of nutrition and they seem to view this field and its problems in a superficial way. One of them is a physiologist and cardiologist; another is somewhat harder to classify but in this report he writes like an epidemiologist. Both are experienced poultry men. These circumstances lead to several unsound statements and interpretations.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

The Life and Times of Sir Charles Hastings, Founder of the British Medical Association. By William H. McMenemey, M.A., D.M., F.R.C.P. Boards. $10. Pp. 516, with illustrations. [Williams & Wilkins Company, 428 E. Preston St., Baltimore 2]; E. & S. Livingstone, Ltd., 16 and 17 Teviot Pl., Edinburgh 1, Scotland, 1959.

This is the biography of the man who in 1832 founded the Provincial Medical and Surgical Association in Worcester, the oldest association of general practitioners in England. Since this later merged with other local medical societies to form the British Medical Association, Hastings is credited with being its founder. In those days as in modern times there were many heated controversies involving medical standards, general policy, and laws related to medical practice. Hastings took an active part in all such matters and for many years served as a secretary of the Provincial association. The style of this biography is leisurely, and it should appeal to those who have a special interest in medical history. Furthermore, in anyone who has lived in the Midlands it is sure to awaken pleasant memories. At the end of the volume there is a bibliography of Hastings' writings, a general bibliography, and an index.

Medical Department, United States Army. Cold Injury, Ground Type. By Colonel Tom F. Whayne, Professor of Preventive Medicine, School of Medicine, University of Pennsylvania, Philadelphia, and Michael E. DeBakey, M.D., Professor of Surgery and Chairman of Department, Baylor University College of Medicine, Houston. Prepared under direction of Major General S. B. Hays, Surgeon General, United States Army. Editor in chief: Colonel John Boyd Coates, Jr. Associate editor: Elizabeth M. McFetridge, M.A. Office of Surgeon General, Department of Army, Washington, D. C. Cloth. $6.25. Pp. 570, with illustrations. Superintendent of Documents, Govern. Print. Off., Washington 25, 1958.

This book, one of the volumes which comprise the official history of the medical department of the United States Army in World War II, is essentially a history of the experience with cold injuries encountered in the various theaters of operations. There is little doubt that the statement in the foreword "that this is the most comprehensive volume on the ground type of cold injury that has ever been published" is correct. The further statement that, if the experience here recorded is given due consideration there should be no similar experience in future wars, seems equally well-founded. The book is beautifully illustrated and written in a most interesting manner. The reader will be staggered at the magnitude of disability caused by cold injury during World War II, and at the multiple problems of supply of clothing and distribution of infor-

mation which led to the development of this experience. No attempt is made to whitewash the many errors in judgment made by high-ranking officials which seem altogether obvious in retrospect. The armchair tactician should find the correlation of battle circumstances with the development of cold injuries most interesting.

A number of the chapters should be of particular interest to the nonmilitary physician. Those on General Consideration of Cold Injury, Pathogenesis and Pathologic Process, Clinical Picture and Diagnosis, Therapy and Disposition Overseas, and Therapy and Disposition in Zone of the Interior should be of great value to any physician treating cold injuries. A particularly noteworthy portion of the book is that which deals with cold injuries incurred at high altitudes. The state of our knowledge concerning these injuries is far from complete, and the current answer to the problem lies in prevention rather than treatment of these lesions. This volume should be required reading for the military surgeon as well as for persons in positions of command in the armed forces.

Youth and Fitness: A Program for Secondary Schools. Report of National Conference on Fitness of Secondary School Youth, December 7-12, 1958, Washington, D. C. Paper. $1.50; discounts on quantity orders. Pp. 74, American Association for Health, Physical Education, and Recreation, a department of National Education Association, 1201 16th St., N. W., Washington 6, D. C., 1959.

This report of a conference sponsored by the American Association for Health, Physical Education, and Recreation includes the keynote address by Shane MacCarthy, executive director of the President's Council on Youth Fitness, and a speech by Wayne O. Reed, deputy commissioner of the U. S. Office of Education. There are special groups of recommendations in relation to health education, physical education, boys athletics, girls physical activity program, recreation in general, and outdoor education. Other contributions were "The Social and Economic Setting for American Education" by Marion Clawson of the Ford Foundation; "Advances in Health and Medical Sciences" by Aims C. McGuinness, M.D., assistant to the secretary of the U. S. Department of Health, Education, and Welfare; "The Growth and Development of Today's Adolescent" by Prof. John J. Kurtz of the University of Maryland; and "The Role of the American Secondary School" by Paul E. Elicker, executive secretary of the National Association of Secondary School Principals.

Although the purpose of the conference included the discipline of medicine and its representation along with public health, recreation, athletics, and child growth and development, a check of the list of participants reveals only three physicians. The medical aspects of the various subjects covered are touched on only sketchily. The section on physical education, for example, contains among the essentials of a desirable physical education program sections on attitudes, knowledge, skills, administrative provisions for physical education, and general recommendations, but no reference to the importance of medical examination for athletes or participants in physical education or the importance of injury prevention or emergency service to injured or ill participants.

Office Orthopedics. By Lewis Cozen, M.D., F.A.C.S., Attending Orthopedic Surgeon, Cedars of Lebanon Hospital, Los Angeles. Third edition. Cloth. $9.50. Pp. 430, with 321 illustrations. Lea & Febiger, Washington Sq., Philadelphia 6, 1959.

This book covers such subjects as physical therapy, legs, arms, back, scoliosis, neck, clubfoot, limp, flat foot, bowlegs, and knock knees. The table of contents is confusing. One might question the inclusion in this book of a discussion of painful jaw. The section on scoliosis is poor and the section on the law court is grossly inadequate. The author's consideration of stellate ganglion block as a routine office procedure is highly questionable. The value of hydrocortisone is overemphasized. Prosthesis fitting is hardly an office procedure. The proof reading is poor. The quality of the illustrations ranges from superb to amateurish. The author's excellent qualifications are not reflected in his book. He fails flagrantly to credit original sources of text and illustrations; he furnishes an extensive bibliography and states that he has read every article listed. It is unbelievable that a man could have read so much good material and still give his readers so little. The book does not fill a need, niche, or vacuum.

The Barbiturate Withdrawal Syndrome: A Clinical and Electroencephalographic Study. By Munke Hertel Wulff. [Thesis, M.D., University of Copenhagen.] Issued simultaneously as Electroencephalog. & Clin. Neurophysiol., supp. no. 14. Paper. Pp. 173, with 19 illustrations. Ejnar Munksgaard, Nørregade 6, Copenhagen, K, Denmark, 1959.

This monograph, the first of its kind, presents useful information for both the clinician and the researcher. The subject matter should appeal to a wide cross section of specialists in both fields. The author deserves credit for collating data on 78 chronically addicted barbiturate users as well as 40 patients who are used for comparison and control. The study represents more than five years of research.

The historical and introductory data are well presented in text and tables without being too lengthy. Throughout the monograph liberal use is made of clearly presented figures and tables. Methods are well described, and the use of controls is notable throughout. The monograph is comprehensive in that clinical, pharmacological, chemical, neuropathological, and electroencephalographic data are included. The idea is presented that the barbiturates which disappear slowly from the blood are less like-

ly to induce major abstinence manifestations on abrupt withdrawal. The use of photic stimulation to induce paroxysmal electroencephalographic changes during withdrawal of barbiturates is presented, and its experimental and clinical utility made apparent.

The final chapter is devoted to conclusions and practical implications. In addition, there is a nine-page summary in Danish. An appendix with selected case studies presented in text and table form is another useful feature. The list of references is comprehensive, and an index is provided. This monograph is unequivocally recommended and should be especially useful to neurologists, psychiatrists, electroencephalographers, and pharmacologists, but the multidisciplinary approach and comprehensive nature of the work give it a flavor which should prove interesting to a wide variety of readers.

Handbook on Standard Nomenclature of Diseases and Operations. By Edward T. Thompson, M.D., editor, Standard Nomenclature of Diseases and Operations, and Adaline C. Hayden, C.R.L., associate editor. Prepared for American Medical Association. Paper. $1.50. Pp. 71. Blakiston Division, McGraw-Hill Book Company, Inc., 330 W. 42nd St., New York 36; 95 Farringdon St., London, E. C. 4, England; 253 Spadina Rd., Toronto 4, Canada, 1959.

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The chief aim of this handbook is to present in simple form the basic principles of terminology and a brief analysis of nomenclature. This booklet can be easily carried in the pocket and should be of special value to the intern and resident. Nothing concerned with the nomenclature of diseases and operations is more important than that an acceptable standard be compiled and used. Unfortunately, differences of opinion among experts and changing concepts of disease necessitate constant reevaluation and revision so that, although we may approach a fixed standard, we can never really achieve it. Insofar as a standard of nomenclature furthers the elimination of obsolete terms and the use of preferred terms on the widest possible scale it will have accomplished a worthy purpose.

As stated in this handbook, "in recording a diagnosis, the physician should make certain (1) that his statement is specific and complete, (2) that he names a disease entity, not a symptom of the disease, (3) that his statement does not contain eponyms or obsolete or indefinite terms, and (4) that he is not using a pathologic statement for a clinical diagnosis." A list of unacceptable eponyms and their corresponding preferred terms is included and should be most valuable. The retention of "acceptable" eponyms is deplorable and an indication that for some diseases exact diagnostic terms are still not generally agreed on. Although most of the material found in this booklet should be incorporated in "Standard Nomenclature of Diseases and Operations," it is well to have this practical handbook. It is hoped that it will be widely used.

Pathology of Tumours of the Nervous System. By Dorothy S. Russell, Sc.D., M.A., M.D., Director, Bernhard Baron Institute of Pathology, London Hospital, London, and L. J. Rubinstein, M.D., Lecturer in Morbid Anatomy, London Hospital Medical College, London. With chapter on Tissue Culture in Relation to Tumours of the Nervous System, by C. E. Lumsden, M.D., Professor of Pathology, University of Leeds, Leeds. Cloth. $13.50. Pp. 318, with 286 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2; Edward Arnold (Publishers) Ltd., 41 Maddox St., London, W. 1, England, 1959.

The author of this volume is one of the world's most outstanding neuropathologists. She has always been forthright in drawing and expressing her conclusions. Even those who have disagreed with her have admired her approach to pathological problems. This is an excellent book. It is concisely and clearly written. It is not encyclopedic, as is the much larger book by Zülch (published as vol. 3 of the "Handbuch der Neurochirurgie" in 1956), but it is adequate. It also contains appropriate bibliographic references. The photomicrographs are well chosen and clearly reproduced. The concluding chapter on tissue culture is a stimulating addition. This technique has never been fully exploited in our study of neoplasms and their treatment, and this intriguing subject is well presented here. Everyone interested in learning about tumors of the nervous system and their pathological characteristics should find this a useful book. It is recommended without reservation.

Immunopathology: 1st International Symposium. Edited by Pierre Grabar and Peter Miescher. [In English, French and German.] Cloth. $16.25. Pp. 520, with illustrations. Benno Schwabe & Co., Steinentorstrasse 13, Basel, Switzerland [Intercontinental Medical Book Corporation, 381 Fourth Ave., New York 16], 1959.

The 50 investigators, immunologists, immunopathologists, immunochemists, and clinicians who participated in this symposium in 1958 talked on inflammation, properdin, agammaglobulinemia, organ-specific immunopathology, rheumatoid arthritis, and disseminated lupus erythematosus. Some of the world's leading authorities in these new and rapidly growing fields of medical research are represented in this volume. The session was opened by Witebsky with a scholarly and sparkling sketch of the history of immunopathology, and he spoke again on his own pioneering contributions in the role of autosensitization in thyroid disease. Another American investigator, Good, spoke on agammaglobulinemia, the condition with which his name is intimately connected. Most of the other speakers were of similarly high caliber. The bulk of the book is taken up by inflammation and lupus erythematosus (160 and 150 pages respectively). For those who did not attend this symposium, reading this well-edited and documented account of what must have been an exciting and stimulating event is the next best thing.

QUESTIONS AND ANSWERS

ANAPHYLACTIC REACTION FROM TRYPSIN

To the Editor:—*An obese middle-aged woman with hypertension had been treated by another physician for a varicose ulcer of the left leg, over the tibia. Improvement over a 10-day period with use of an ointment was slow. Her ulcer became redder and more painful. I was then consulted, and I gave her an injection of 1 cc. of aqueous chymotrypsin (Chymar, 5,000 units). She had a history of a moderate reaction to penicillin. She felt very hot four or five minutes after the injection. Her blood pressure at this time was 158/92 mm. Hg. She said she felt dizzy. Simple syncope was suspected. In the next two minutes the patient felt worse and thought she would faint. She also had difficulty breathing. Her radial pulse became barely palpable and rotary nystagmus developed.*

At this time 100 mg. of hydrocortisone was injected into the site of the earlier injection. The radial pulse disappeared and the patient lost consciousness. Three or four minutes later the patient became semiconscious. Her body became covered with circular hives. Investigation at the local pharmacy showed the ointment prescribed by the first physician to be crystalline trypsin ointment (Tryptar). What is the incidence of severe sensitization to parenterally given trypsin subsequent to its topical use? How permanent is such an allergic response?

Martin L. Hauer, M.D., Lebanon, Pa.

Answer.—The ointment used contains a purified crystallized trypsin derived from mammalian pancreas. Sensitization or antigenicity to this preparation has not been reported. According to the manufacturer, it may exhibit a histamine-like effect which is easily controlled by antihistaminics. Despite this description, the sequence of events in this patient strongly points to the probability that the ointment was antigenic in nature. Since the trypsin is derived from mammalian pancreas, it certainly is a foreign protein. The sensitizing factor may be the protein of the animal whose pancreas was used in preparation of the trypsin or the pancreatic tissue protein itself.

It is likely that the repeated application of the trypsin ointment in an ulcerated area over a period of 10 days was sufficient to sensitize this patient so that subsequent injection of chymotrypsin was enough to produce anaphylactic shock. The manufacturer indicates in describing Chymar that "although sensitivity is uncommon the usual precautions should be exercised in those patients with known allergies or sensitivity."

Once present, it is difficult to define exactly the duration of such sensitivity. It may persist; hence such a person's life might be endangered by inadvertent prolonged parenteral use of chymotrypsin. Two cases reported by Criep (*J. Allergy* **12**:154, 1941) indicate a shorter duration. A systemic allergic reaction occurred after the intramuscular injection of deinsulinized pancreatic tissue. Treatment was resumed after an interval of a month in one instance with but one untoward reaction, and it was subsequently continued every three or four days for a month without any symptoms. In the other case therapy was discontinued for two months after a rather mild reaction to the injection of pancreatic extract and subsequently was restarted without any trouble. Thus each case has to be evaluated individually and every precaution taken, especially if the patient is constitutionally allergic.

The fact that a protein substance has its analog in the human does not mean it is not a totally foreign protein. Human beings may become sensitized to their own tissues, which may act as foreign proteins when altered by infection or chemical agents.

NORMAL PROTEINURIA

To the Editor:—*What is the upper limit of normal of proteinuria in the healthy adult? Orthostatic albuminuria has been ruled out, and there is no history of genitourinary disease. The sulfosalicylic acid reagent test method has been used.*

M.D., North Carolina.

Answer.—The glomerular filtrate of the kidneys normally contains about 25 mg. of protein per 100 ml.; the 180 liters of glomerular fluid filtered during the course of one day would contain 45 Gm. of protein. Addis (Glomerular Nephritis: Diagnosis and Treatment, New York, the Macmillan Company, 1949) estimated the normal protein excretion to be from 5 or 10 to 100 mg. per 24 hours. Rigas and Heller (*J. Clin. Invest.* **30**:853, 1951), by ultrafiltration concentration of the urine, found an average of 40 mg. of protein per 24 hours. For convenience, the daily urine volume can be assumed to be 1,000 ml., resulting in a normal concentration of 0.5 to 10 mg. of protein per 100 ml. The sulfosalicylic acid test for proteinuria is sensitive

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enough to give a "faint trace" positive at 10 to 50 mg. per 100 ml. The heat and acetic acid test is more sensitive, detecting 1 to 3 mg. per 100 ml. in "clear" urine against a black background; 1 to 10 mg. per 100 ml. is the usual range giving the "very faint trace" positive. Thus, any positive result with sulfosalicylic acid denotes excess protein in the urine, if the daily urine output has been more than 1,000 ml. This test is used as the method of choice (using quantitative standards) by most life insurance companies.

King (*J. A. M. A.* **155**:1023-1026 [July 17] 1954; *Ann. Int. Med.* **42**:296, 1955) has reported on over 5,000 young males referred to an Army hospital because of proteinuria. Using his screening procedure of "serial urine protein excretion" over a period of 18 hours, he has concluded that continuous proteinuria indicates significant organic renal disease. Spiro (*Am. J. Path.* **35**:47, 1959), utilizing the electron microscope, has shown that the structural basis for proteinuria in renal disease is the presence of gaps in the basement membrane of the glomerulus. For routine use, the need is not for a more sensitive test but rather for recognition of conditions that may cause false-positive results (e. g., with the sulfosalicylic acid test). Examples of such conditions are (1) dehydration, (2) less than 1,000 ml. urine output for the day, (3) many bacteria and/or large amounts of amorphous urates, (4) condition after use of iodine-containing drugs for cholecystography, and (5) condition during treatment with tolbutamide due to the metabolite, 1-butyl-3-p-carboxyphenylsulfonylurea.

SECONDARY ADRENAL INSUFFICIENCY

To the Editor:—*What is the effect of cortisone and ACTH on atrophy or hypertrophy of the adrenals? What is the advisability of alternating ACTH with cortisone when therapy is continued for any length of time?*

C. D. Klaus, M.D., Iron Mountain, Mich.

Answer.—When ACTH is given, hyperplasia of the adrenal cortex occurs, with an extensive production of hydrocortisone in addition to small amounts of corticosterone, estrogens, and androgens. Maximal ACTH stimulation produces about 10 mg. of hydrocortisone per hour. There is only a temporary secretion of aldosterone during ACTH stimulation, after which time aldosterone secretion is independent.

If administration of ACTH is stopped suddenly, a lag phase of five to seven days' duration occurs before the pituitary-adrenal system recovers. It is during this time that the patient is in a relative state of adrenocortical insufficiency and an adrenal crisis may develop should he be subjected to stress, such as a severe infection, operation, or injury. The lag phase after ACTH therapy is much shorter than that after therapy with cortisone and its derivatives. The reason for this difference is that the corticosteroids depress the pituitary as well as the adrenal cortex. Deaths of patients have resulted when ACTH and cortisteroid therapy has been stopped abruptly during stress such as trauma, infection, or when an operation is contemplated.

When cortisone, hydrocortisone, or their derivatives are given for several weeks, the lag phase may be as long as six weeks to a year after therapy is stopped. The question often arises as to whether one encounters a permanent irreversible suppressive effect on the pituitary adrenocortical system from prolonged corticosteroid therapy. To date, there is no evidence of such an effect. Unless there has been damage to the pituitary or the adrenal cortex, the adrenal will respond to exogenous ACTH and eventually the pituitary production of ACTH will occur. The reduction of ACTH and corticosteroid therapy should be gradual and cover a period of several weeks. The last dose of corticosteroid therapy should be the morning one. There is no advantage in giving ACTH along with cortisone or its various derivatives.

EFFECT OF FOOD ON LABORATORY TESTS

To the Editor:—*May liquids or food be given to patients who are to have blood chemistry tests?*

Murray W. Shulman, M.D., Irvington, N. J.

Answer.—All physiological investigations should begin with the experimental subject under some basic conditions. In clinical practice it is difficult to satisfy such conditions, but much can be accomplished by withholding food and limiting fluids for a period of time preceding the withdrawal of blood for chemical tests. Most textbooks on clinical pathology advise such a procedure; usually blood is withdrawn before breakfast. The following quotations are examples of this restrictive imposition:

"The concentration of various constituents of the blood is materially altered for a time after meals, and it is therefore necessary, for the sake of uniform results, to obtain the blood after a twelve hour fast, that is, before food is taken in the morning" (Todd, Sanford, and Wells: Clinical Diagnosis by Laboratory Methods: Working Manual of Clinical Pathology, ed. 12, Philadelphia, W. B. Saunders Company, 1953).

"As a general rule digestion has a profound influence upon most of the chemical constituents of the blood requiring that the latter should usually be taken after a period of fasting and preferably in the morning before breakfast" (Kolmer: Clinical Diagnosis by Laboratory Examinations, ed. 2, New York, Appleton-Century-Crofts, Inc., 1949).

Besides the alteration in chemical constituents of the blood brought about by various types of food, the presence of postprandial opalescent serum is a disadvantage in performance of some procedures, such as determinations of serum bilirubin, calcium,

and sulfobromophthalein levels. There also is the problem of keeping burners in flame photometers clean when any particulate or heavy lipoidal material is present. It is impracticable to attempt to control what patients may eat before a test; blood lipids are particularly susceptible to changes caused by intake of fats, and tests for glucose are affected by the ingestion of carbohydrates. Determinations of chloride, urea, nonprotein nitrogen, carbon dioxide–combining power, creatinine, and transaminase values are not particularly influenced by the ingestion of food.

In general, a procedure that calls for no food intake for 6 to 12 hours before blood is to be obtained for chemical determinations will yield results far more consistent than if food were allowed to be taken. In some instances the intake of food will result in erroneous and misleading results of such tests. For example, blood for chemical tests frequently is withdrawn at the same time that specimens of serum are taken for flocculation and complement-fixation tests and that blood is taken for the determination of hemoglobin level. Serious errors can result in the latter determination in the presence of opalescence if a photometer is used; similarly, an excess of lipids in the serum may affect serologic results.

EFFECTS OF STEROIDS ON BRAIN

To the Editor:—*Please supply any available information on effects on the central nervous system of adrenocortical steroid and related therapy.*

Roy J. Ward, M.D., Worcester, Mass.

Answer.—Clinically, large doses of ACTH, cortisone, hydrocortisone, prednisone, prednisolone, triamcinolone, and dexamethasone produce such divergent psychological reactions as euphoria, psychoses, and suicidal depressions. Rome and Braceland (*J. A. M. A.* **148**:27-30 [Jan. 5] 1952) related the type of reaction to the patient's personality and found that psychotic reactions tend to occur in patients whose psychological adjustments are marginal. Psychosis is often preceded by restlessness, tension, and insomnia, which are indications for reduction of dosage, or, if this is not possible, administration of tranquilizer drugs.

This group of adrenocortical steroids is also capable of inducing convulsions, in contrast to desoxycorticosterone acetate, which is an anticonvulsant agent (McQuarrie and others: *J. Clin. Endocrinol.* **2**:406, 1942; Aird and Gordan: *J. A. M. A.* **145**:715-719 [March 10] 1951). Experimentally, the anti-inflammatory steroids lower the threshold to electroconvulsive shock, while desoxycorticosterone raises it (Woodbury: *Recent Prog. Hormone Res.* **10**:65, 1954). Smaller replacement doses of cortisone abolish the electroencephalographic abnormalities of adrenal cortical hypofunction (Addison's disease) (Thorn and co-workers: *Tr. A. Am. Physicians* **62**:233, 1949) and of congenital virilizing adrenocortical hyperplasia (Bartter and associates: *J. Clin. Invest.* **30**:237, 1951).

Curiously, no alteration in cerebral metabolic pattern is found after administration of large doses of ACTH, even during ACTH-induced psychosis (Schieve and others: *J. Clin. Invest.* **30**:1527, 1951), although other steroids with prominent central nervous system activity exert profound cerebral metabolic effects (Gordan: *Recent Prog. Hormone Res.* **12**:153, 1956).

OPERATION IN POSTPARTUM PERIOD

To the Editor:—*Please comment on the feasibility of doing vein strippings in the immediate (e. g., three-to-four-day) postpartum period. The need for operation has been properly established. The reason for this type of management is primarily economic (to avoid another hospitalization).*

Wallace C. Ellerbroek, M.D.
Long Beach, Calif.

Answer.—This consultant knows of no large series of cases in which multiple vein ligations and stripping have been performed in the early postpartum period. Such a procedure can be safely undertaken between pregnancies or during pregnancy up to the seventh month without encountering any difficulty. In the early postpartum period the mother's glandular system, clotting mechanism, and adaption to stress are by no means restored to normal. The stress of a two-to-three-hour-long anesthesia and that of the procedure itself does not seem justified. Breast feeding would be another complication. The economic factor here would be a poor indication for performing an elective operation. Emergency operations, of course, must be performed any time in the postpartum period. The risk of withholding operation in case of a ruptured viscus needs no statistical analysis. Elective operations in the immediate postpartum period, however, unless a minor procedure done with use of local anesthesia, should be postponed for at least three months after delivery.

MULTIPLE MYELOMA

To the Editor:—*Please comment on treatment for multiple myeloma in a 72-year-old man. The diagnosis has been confirmed by bone marrow study.* *James S. McBride, M.D., Indianapolis.*

Answer.—Multiple myeloma is a uniformly fatal disease. There is no known cure. The average duration of life from onset of symptoms is approximately two years, although an occasional patient has survived for 5 or even 10 years. Treatment is palliative by irradiation and administration of urethane. Irradiation is used to treat any bone

lesions that are symptomatic and demonstrated on skeletal survey. For its systemic effect urethane is given as follows: Start with 1 Gm. per day for two or three days, then 2 Gm. per day for two or three days, and so on until 5 Gm. per day is attained, if the patient will tolerate this large dosage. Keep up this regimen until a total of 150 Gm. has been given; then revert to a daily dose of 1 or 2 Gm., depending on the white blood cell count. If the count is about 2,000 per cubic millimeter, give 1 Gm. per day; if it is 6,000 or 7,000 per cubic millimeter, give 2 Gm. per day. This maintenance dosage is continued indefinitely, even for several years.

FISH IN LOW-FAT DIETS

To the Editor:—*Please give answers to the following questions. In the treatment of coronary artery disease, is the degree of exclusion of fish oils and fats in the diet the same as for animal fats? Would this include only the more fatty fish such as salmon, mackerel, and whitefish? In a patient on a low-fat diet, is the ingestion of small amounts (less than 2 oz. daily) of corn oil or the newer corn-oil margarines of any value? Is the ingestion of these small amounts of corn oil of any harm?*

M.D., New York.

Answer.—In the treatment of coronary artery disease with a low-fat, low-cholesterol diet, the incorporation of large amounts of fish of any kind is considered desirable and beneficial. It has been shown in clinical trials that the addition of fish and corn oil decreases serum cholesterol levels below those achieved with a low-fat, low-cholesterol diet alone. The addition of up to 2 oz. of corn oil to such a diet should be allowed only if obesity is not a problem or after weight reduction has been achieved in obese individuals. In using corn-oil margarines, only those which are not hydrogenated can be recommended. While it is advisable to use such a harmless hypocholesteremic regimen, it is only fair to state that this is on the logical assumption that lowering the blood cholesterol level will benefit clinically manifest atherosclerosis—which is as yet unproved.

NEOSTIGMINE IN ALLERGIES

To the Editor:—*What are the dangers of giving neostigmine to a patient who is known to have had allergies and/or asthma? The drug is being considered for testing a patient for myasthenia gravis and for treatment of paroxysmal auricular tachycardia.*

M.D., New York.

Answer.—Any symptoms which would follow the administration of neostigmine to a patient who is allergic, and especially to an asthmatic, would be the result of its pharmacological action and not because of an abnormal, untoward, or allergic reaction. There is apparently no recorded case report of allergy to neostigmine. Therefore, this possibility offers no problem in the asthmatic patient. However, neostigmine may induce an attack of asthma or aggravate a previously existing one because of its pharmacological action. Neostigmine is a cholinesterase inhibitor. Given in large enough dosage, it may induce bronchospasm by allowing sufficient acetylcholine to accumulate to act on the bronchial musculature. But in testing a patient for myasthenia gravis or in treating one with paroxysmal auricular tachycardia, the dosage used probably would be insufficient to induce an asthmatic attack. Its administration in these circumstances therefore should be safe.

PRENATAL CARE AND FLUORINE

To the Editor:—*Is fluorine used in the form of sodium fluoride beneficial in the development of baby teeth in utero? Is it indicated for prenatal care?*

M.D., Massachusetts.

Answer.—There is little evidence to suggest that low levels of fluorides can pass the placental barrier. In any case, the formation of prenatal enamel is so perfect that addition of fluoride in prenatal care is not indicated.

SURGERY OF CECAL TUMOR

To the Editor:—*A 55-year-old man was operated on for acute appendicitis and a mass was found in the base of the cecum. The differential diagnosis was carcinoma of the cecum or cecal diverticulitis. Is it possible to make the diagnosis on a gross examination? Should the cecum be opened to view the mucosa? Should an ileocolic resection be performed when the exact diagnosis is not certain? If the diagnosis is presumed to be cecal diverticulitis, what is the proper treatment?*

M.D., New York.

Answer.—It is not possible in all abdominal explorations to determine whether cecal masses are benign or malignant. The colon should not be opened for the sole purpose of viewing the mass, and the right half of the colon and terminal portion of the ileum should not be resected unless obstruction is present. In the absence of obstruction, a cecal diverticulum may be removed in a manner similar to removal of an appendix, unless it has become acutely inflamed and involves the cecum (in such cases the correct diagnosis cannot be made). The initial incision should be closed, the patient prepared with antibiotics, and a second operation performed six to seven days later. If the mass persists, a resection would be in order.

DIAGNOSIS OF HERNIA

To the Editor:—*A middle-aged man with dilated external inguinal rings has been told that he has a direct hernia. Examination shows no protrusion through the external ring, but the palpating finger can detect a definite impulse in the posterior wall of the inguinal canal. I feel that this is more or less normal for men of that age, but it has raised a point as to when a direct hernia can be classified as such.* *M.D., Pennsylvania.*

Answer.—Most writers on the subject seem to agree that a hernia must be thought of as a defect or a hole in the abdominal wall through which abdominal contents may protrude. This opening may be an abnormal one or a pathological enlargement of a normal aperture. A weak point or actual defect in the abdominal wall through which no content has as yet protruded may be thought of as a potential hernia. A definite sac is not necessary to establish existence of a hernia. In direct hernia, the fundamental cause of the hernia is a weakness of the abdominal musculature. There is a deficiency in the inguinal triangle (lower margin of the internal oblique muscle above, rectus sheath medially, and the inguinal ligament below). If such a defect is present and if a sac protrudes through this defect, the patient has a direct hernia.

CARE OF CHRONIC ULCERS

To the Editor:—*Has the following combination treatment for deep ulcers, sinus tracks, gangrenous lesions, bedsores, or other chronic lesions ever been published? 1. Apply proteolytic enzymes—combined streptokinase and streptodornase or trypsin and chymotrypsin. 2. Apply iodochlorhydroxyquin (Vioform) powder. 3. Apply granulated sugar. 4. Use dry dressing if necessary. There is rapid lysis of old debris in a few days, all infection disappears, and rapid healing occurs.* *Joe C. Gilbert, M.D., Lebanon, Pa.*

Answer.—The method submitted apparently has not been published as a combination treatment. Doubtless many superficial ulcers and sinus tracks would be benefited by such treatment. Innumerable medicaments such as the above have been used on chronic leg ulcers secondary to varicosities or thrombophlebitis without resulting in healing, however. It is the consensus of vascular surgeons that such ulcers should be widely and deeply excised, the varicosities eradicated, and the defect covered with skin grafts. Gangrene of the toes or feet secondary to marked arterial insufficiency also does not usually respond to such measures but requires some specific aid to circulation.

POSTPARTUM HAIR PROBLEMS

To the Editor:—*A postpartum patient complained at six weeks of complete loss of all curl in her hair. Previous to this pregnancy, her hair had a natural wave. A permanent wave was attempted but produced absolutely no effect. Please give information on the cause and treatment.*

Sheldon M. Biback, M.D., Seattle.

Answer.—Women who have trouble with the hair after childbirth are usually anemic, hypoproteinemic, or both. Diffuse hair loss is common; spontaneous regrowth may be expected after a few months. A hypothyroid state may follow parturition, influencing hair nutrition, texture, and responsiveness to cosmetic physiochemical procedures. The effect of fatigue on the mother of a new baby also appertains. The measures likely to bring about a return to normal include a diet high in protein; the restriction of caffeine, because it only masks fatigue; a plan for enabling the woman to secure adequate rest; the administration of a suitable hematinic; and the correction of hypothyroidism, if it is present.

SAFETY OF PETROLATUM ON SKIN

To the Editor:—*Will petrolatum jelly applied to the skin daily over a protracted period of time, such as years, be harmful either as a potential carcinogen or because of possible effects on skin glands?* *M.D., New Jersey.*

Answer.—Petrolatum, which is said to be a mixture of semisolid hydrocarbons obtained from petroleum, is considered by most dermatologists to be a safe base for topical application to the skin. There is no good evidence that it can act as a carcinogenic agent or as a photosensitizer or that it has any of the undesirable properties of certain other hydrocarbons. It is doubtful that it could have any adverse effects on the sebaceous or sweat glands.

RADIUM ON WATCH DIALS

To the Editor:—*Is there any danger of radiation from wearing a wrist watch with illuminated dial and hands?* *M.D., West Virginia.*

Answer.—Watches with luminous dials usually contain small amounts of radium painted on the dial numerals and hands. In a recent article, Webster (*Radiology* 72:493, 1959) calculates that if an average watch with a luminous dial is worn continuously, the radiation dose to the gonads would be 20 mr per year. While this amount of radiation is not high, it is significant. In an evaluation of unnecessary exposure to radiation, the radiation from such watches must be considered.